AUGUST, 1946

MEDICAL LIBRARY

SEP 16 1946

Vol. 124, No. 2

ANNALS of SURGERY

A Monthly Review of Surgical Science and Practice

CONTRIBUTIONS IN THIS VOLUME

IN HONOR OF

ALLEN OLDFATHER WHIPPLE

J. B. LIPPINCOTT COMPANY

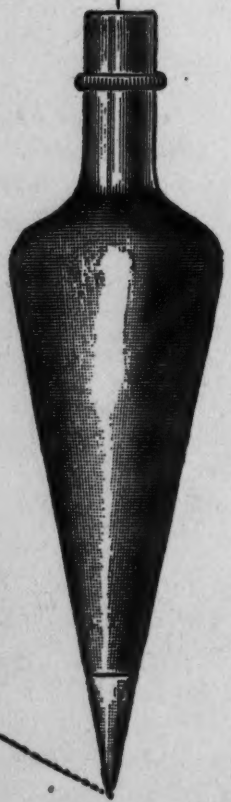
Precision

Of the many types of anesthesia, spinal procedures are the most exacting in their requirements. Because of its pharmacological precision, NEOcaine has demonstrated its fitness for spinal anesthesia over a thirty-year period of clinical use.

In practice, NEOcaine is (1) *always sterile,* (2) virtually flash-soluble in cerebrospinal fluid, (3) stable to epinephrine, (4) rapidly and completely absorbed without irritation and (5) of low toxicity in anesthetic concentrations.

ADMINISTRATION: Employ 1 mg. of NEOcaine per pound of body weight, up to 150 mg. Dissolve crystals with spinal fluid led into the ampoule. Inject slowly with optional barbotage, using a 22 gauge needle. Contraindicated in gastrointestinal perforation, obstruction, peritonitis, severe hypotension, cerebrospinal or dorsal skin disease. Drug idiosyncrasy is rare.

SUPPLIED: Ampoules of 50, 80, 100, 120, 150, 200, 300 mg. of pure procaine hydrochloride. Boxes of 10. For continuous spinal anesthesia, ampoules of 500 mg., individually boxed.



NEOcaine
1917 1946

AMGLO-FRENCH Laboratories, Inc.
75 Varick Street, New York 13, N. Y.

VOL. 124 AUGUST, 1946 NO. 2

ANNALS of SURGERY

A MONTHLY REVIEW OF SURGICAL SCIENCE AND PRACTICE

ALSO THE OFFICIAL PUBLICATION OF THE AMERICAN SURGICAL ASSOCIATION; THE SOUTHERN SURGICAL ASSOCIATION; PHILADELPHIA ACADEMY OF SURGERY; NEW YORK SURGICAL SOCIETY.

EDITORIAL BOARD

WALTER E. LEE, M.D.
Chairman, *Philadelphia, Pa.*

BARNEY BROOKS, M.D.
Nashville, Tenn.

E. D. CHURCHILL, M.D.
Boston, Mass.

EVARTS A. GRAHAM, M.D.
St. Louis, Mo.

ROSCOE R. GRAHAM, M.D.
Toronto, Canada

SAMUEL C. HARVEY, M.D.
New Haven, Conn.

ROY D. McCLURE, M.D.
Detroit, Mich.

GEORGE P. MULLER, M.D.
Philadelphia, Pa.

H. C. NAFFZIGER, M.D.
San Francisco, Cal.

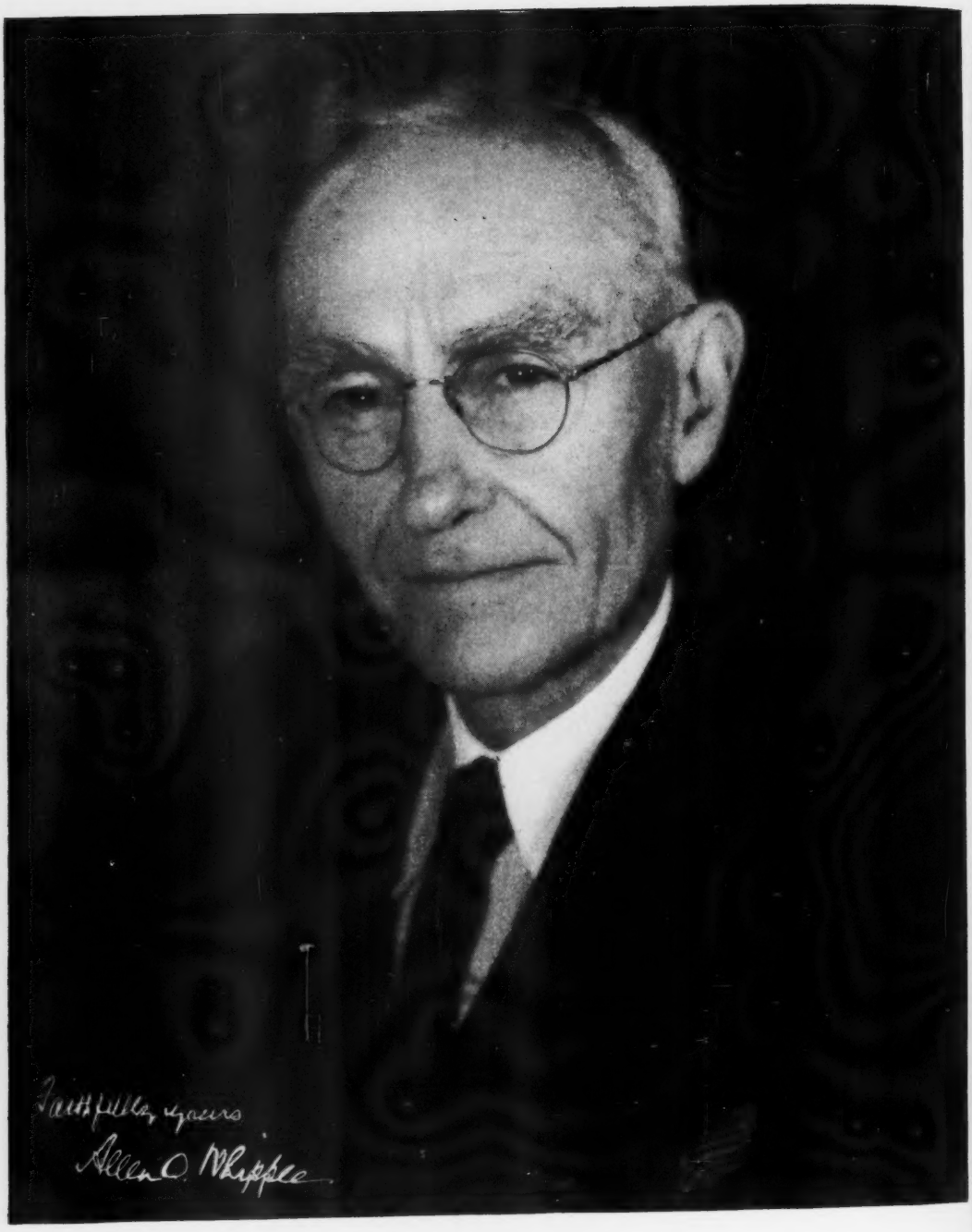
D. B. PHEMISTER, M.D.
Chicago, Ill.

W. F. RIENHOFF, JR., M.D.
Baltimore, Md.

A. O. WHIPPLE, M.D.
New York, N. Y.

JAMES TAFT PILCHER, M.D., Managing Editor

J. B. LIPPINCOTT COMPANY, *Publishers*
PHILADELPHIA MONTREAL LONDON NEW YORK



ALLEN OLDFATHER WHIPPLE

ANNALS OF SURGERY

VOL. 124 AUGUST, 1946 No. 2

IN HONOR OF

ALLEN OLDFATHER WHIPPLE

THE year nineteen hundred and forty-six marks the completion of twenty-five years of service for Allen Oldfather Whipple as the Valentine Mott Professor of Surgery at the College of Physicians and Surgeons, School of Medicine, Columbia University, and a Director and Attending Surgeon, Presbyterian Hospital and Vanderbilt Clinic, New York City.

In the field of Surgery his clinical and experimental contributions are outstanding. As a teacher of medical students and surgeons his influence has been far-reaching. As a leader and coördinator of studies of surgical problems of World War II he brought his broad knowledge of Anatomy, Physiology and Pathology with important results.

To his many associates and friends, however, he has endeared himself most by his qualities of gentleness, integrity and devotion to his profession.

As an appreciation of his leadership, and as an expression of their admiration and affection, the Interns, Residents and Fellows who have worked under his direction for these past twenty-five years, are among those who contribute to this volume.

APGAR, VIRGINIA
CADMAN, EDWARD F.
CANAVARRO, KIM
CHILDS, SAMUEL D., JR.
CLEVELAND, MATHER
DEERY, EDWIN M.
ELLIOTT, R. H. E., JR.
FRANTZ, VIRGINIA KNEELAND
GOODMAN, EDWARD
HAAGENSEN, C. D.
HAGGART, G. EDMUND
HARVEY, HAROLD D.
HEINBECKER, PETER
HOGG, BRUCE M.
HOWES, EDWARD L.
HUDACK, STEPHEN S.
HUMPHREYS, GEORGE H.
LEIGH, OCTA C.
LOCKWOOD, JOHN S.
McALLISTER, FERDINAND F.
McDONALD, JOSEPH J.
McLAUGHLIN, HARRISON L.
MEADE, RICHARD H., JR.
MOORE, RICHMOND L.
PENFIELD, WILDER
POOL, J. LAWRENCE
PULASKI, EDWIN J.
RENNIE, JAMES W. R.
SCUDDER, JOHN
SMITH, FREDERICK M.
SMITH, J. ROY
STIMSON, BARBARA
TAYLOR, FREDERIC W.
WEBSTER, GEORGE V.
WYLIE, ROBERT H.

CONTRIBUTORS

APGAR, VIRGINIA, M.D
Associate Professor of Anesthesia, The Presbyterian Hospital, New York City.

CANAVARRO, KIM, LIEUT.
Medical Corp, United States Army.

CHILDS, SAMUEL D., JR., M.D.
Denver, Colorado.

CLEVELAND, MATHER, COL., M.C.
New York City.

DEERY, EDWIN M., M.D.
Attending Neurosurgeon, New York Orthopedic Hospital, New York City.

ELLIOTT, ROBERT H. E., JR., M.D.
Instructor in Surgery, Columbia University, New York City.

FRANTZ, VIRGINIA KNEELAND, M.D.
Assistant Professor of Surgery, Columbia University, New York City.

GOODMAN, E. N., M.D.
Instructor in Surgery, Columbia University, New York City.

HAAGENSEN, C. D., M.D.
Assistant Professor of Surgery, Columbia University, New York City.

HAGGART, G. EDMUND, M.D.
Lahey Clinic, Boston, Massachusetts

HARVEY, HAROLD D., M.D.
Assistant Professor of Clinical Surgery, Columbia University, New York City.

HEINBECKER, PETER, M.D.
Associate Professor of Clinical Surgery, Department of Surgery, Washington University School of Medicine, St. Louis, Missouri.

HOGG, BRUCE M., M.D.
Instructor in Surgery, The Presbyterian Hospital, New York City.

HOWES, EDWARD L., M.D.
Associate Clinical Professor of Surgery, Columbia University, New York City.

HUDACK, STEPHEN, M.D.
Associate Professor Orthopedic Surgery, Columbia University, New York City.

HUMPHREYS, GEORGE, M.D.
Valentine Mott Professor of Surgery, Columbia University, New York City.

LEIGH, OCTA C., M.D.
Instructor in Surgery, Columbia University, New York City.

LOCKWOOD, JOHN, M.D.
Associate Professor of Surgery, Yale University.

MCALLISTER, FERDINAND F., M.D.
Assistant Resident, The Presbyterian Hospital, New York City.

McDONALD, JOSEPH J., M.D.
Assistant in Surgery, Columbia University, New York City.

McLAUGHLIN, HARRISON L., M.D.
Assistant Professor of Clinical Orthopedic Surgery, Columbia University, New York City.

MEADE, RICHARD H., JR., M.D.
Chicago, Illinois.

MOORE, RICHMOND L., M.D.
Associate in Surgery, Columbia University, New York City.

PENFIELD, WILDER, M.D.
Professor of Neurology and Neurologic Surgery, McGill University, Montreal, Canada.

POOL, J. LAWRENCE, M.D.
Assistant in Neurology, Columbia University, New York City.

PULASKI, EDWIN J., CAPT., M.C.
Halloran General Hospital, 1258th SCU, Staten Island, New York.

RENNIE, JAMES W. R., M.D.
Winnipeg, Canada.

SCUDDER, JOHN, M.D.
Assistant Professor of Surgery, Columbia University, New York City.

SMITH, FREDERICK M., M.D.
Assistant Professor of Clinical Orthopedic Surgery, The Presbyterian Hospital, New York City.

SMITH, J. ROY, LIEUT., M.C.
Medical Corps, United States Army.

STIMSON, BARBARA, M.D.
Assistant Professor of Clinical Orthopedic Surgery, The Presbyterian Hospital, New York City.

TAYLOR, FREDERIC W., M.D.
Indianapolis, Indiana.

WEBSTER, GEORGE V., M.D.
Pasadena, California.

WYLIE, ROBERT, M.D.
Associate in Surgery, Columbia University, New York City.

DUE TO LIMITATIONS OF SPACE, THE PAPERS OF THE FOLLOWING CONTRIBUTORS APPEAR BY TITLE ONLY

HOWORTH, BECKETT, M.D.
Associate in Orthopedic Surgery, New York Orthopedic Hospital, New York City.
CONGENITAL DISLOCATION OF THE HIP.

SCUDDER, JOHN, M.D.
Assistant Professor of Surgery, Columbia University, New York City.
ELECTROPHORETIC PATTERNS IN EXTENSIVE BURNS.

SMITH, BEVERLY C., M.D.

Associate in Surgery, Columbia University, New York City.

THE USE OF RADIOACTIVE SODIUM IN THE STUDY OF PERIPHERAL VASCULAR DISEASE.

STEVENSON, THOMAS W., M.D.

Associate in Surgery, Columbia University, New York City.

RECONSTRUCTION OF THE ESOPHAGUS BY A SKIN LINED TUBE.

WEBSTER, JEROME P., M.D.

Assistant Professor of Clinical Surgery, Columbia University, New York City.

MASTECTOMY FOR GYNECOMASTIA THROUGH A SEMICIRCULAR INTRA-AREOLAR INCISION.

BIBLIOGRAPHY OF DR. ALLEN O. WHIPPLE

The Development of the Blastoderm of the Chick in Vitro. Anat. Record, **6,** 121–139, March, 1912. (With McWhorter, J. E.)

A Study of Postoperative Pneumonia in the Presbyterian Hospital during 1915. Med. Record, N. Y., **89,** 581, 1916.

A Study of One Hundred Consecutive Fractures of the Shafts of Both Bones of the Forearm with the End-results in Ninety-Five. Surg., Gynec. & Obst., **25,** 77–91, July, 1917. (With St. John, F.B.)

Double Transverse Incision. Med. Record, N. Y., **93,** 437, 1918.

Suppurative Nephritis with Calculus in Ureter. Am. Surg., **67,** 755, 1918.

Diseases of the Biliary Tract and Pancreas. ANNALS OF SURGERY, **68,** 107–109, 1918.

A Study of Postoperative Pneumonitis. Surg., Gynec. & Obst., **26,** 29–47, January, 1918.

History Analysis Applied to Surgical Diseases of the Biliary Tract and Pancreas. ANNALS OF SURGERY, **68,** 471–484, November, 1918.

The Diagnostic Use of the Duodenal Tube. ANNALS OF SURGERY, **73,** 556, May, 1921.

Pancreatic Asthenia. ANNALS OF SURGERY, **78,** 176, August, 1923.

Certain Factors in the Differential Diagnosis of Nonacute Lesions of the Stomach, Biliary Tract and Appendix. Trans. of Inter-State P.G. Med. Asso., 1923.

Immediate Mobilization after Aseptic Arthrotomy as Compared with Immobilization. Am. Jour. Surg., **39,** 49, March, 1925.

Hemorrhage from Gastric and Duodenal Ulcer: Case Reports. Surg. Clin. of N. A., **5,** 583–619, April, 1925.

A Study of Subdiaphragmatic Abscess: An Analysis of 32 Cases. Am. Jour. Surg., **40,** 1, January, 1926.

The Adaptation of Medical Education to Changing Clinical Practice. The Proceedings, Congress on Medical Education, Licensure, Public Health and Hospitals, February, 1926.

Splenectomy as a Therapeutic Measure in Thrombocytopenic Purpura Hemorrhagica. Surg., Gynec. & Obst., **42,** 329–341, March, 1926.

Surgical Criteria for Cholecystectomy. Am. Jour. Surg., **40,** 129, June, 1926.

More Recent Studies upon the Etiology of the Postoperative Pneumonitis. N. Y. State Jour. Med., **26,** 967, December, 1926.

Lesions of the Liver Amenable to Surgical Therapy. Am. Jour. Surg., January, 1927.

Diseases of the Pancreas. Cecil Textbook of Medicine. Wm. B. Saunders Co., Philadelphia, 1927.

The Relation of the Reticulo-endothelial System to the Splenomegalies Associated with Nonspecific or Secondary Anemia. New Orleans Med. & Surg. Jour., **79,** 800–815, May, 1927.

Side-tracking Operations for Common Duct Obstruction. ANNALS OF SURGERY, **86,** 540, October, 1927.

Surgery of the Biliary Tract. Nelson's Loose-Leaf Living Surgery, Vol. 5, Chap. 9. Thomas Nelson & Sons, 1928.

Atypical Hemolytic Anemia with Splenomegaly in Children. ANNALS OF SURGERY, **87,** 380–387, September, 1928. (With Reeves, R. J., and Cobb, C. C.)

The Clinical Course of Subacute Yellow Atrophy: As Observed in Two Proven Cases. Am. Jour. Surg., **6,** 655–661, May, 1929.

The Surgical Treatment of the Bile Typhoid Carriers. ANNALS OF SURGERY, **88,** 631–642, October, 1929.

Clinic of Dr. Allen O. Whipple: Stones in Common and Cystic Bile Ducts, 249–252; *idem. ibid.:* Results of Short-circuiting Procedures for Common Duct Obstruction, 253–256. 1930. Clinical Congress of the American College of Surgeons.

Acute Infections of the Gallbladder and Biliary Tract. Bull. N. Y. Acad. of Med., **7,** 211–220, March, 1931.

Advantages of Cecostomy Preliminary to Resections of Colon and Rectum. J. A. M. A., **97,** 1962–1963, December, 1931.

Complications Associated with Major Proctectomy. ANNALS OF SURGERY, **91,** 916–922, June, 1932.

The Use of Silk in the Repair of Clean Wounds. ANNALS OF SURGERY, **92,** 662–671, October, 1933.

The Problem of Dealing with the Typhoid Carrier. Puerto Rico Med. Jour., July, 1933.

The Relation of Type and Grade to Operability and Prognosis in Gastric Carcinoma. Puerto Rico Jour. of Public Health & Tropical Med., **9,** 217–227, March, 1934. (With Raiford, Theodore S.)

The Type and Grade of Gastric Carcinoma in Relation to Operability and Prognosis. Surg., Gynec. & Obst., **59,** 397–409, September, 1934. (With Raiford, Theodore S.)

Diseases of the Biliary Tract. Nelson's Loose-Leaf Surgery, "Surveys of Current Literature," Vol. 5, 195–201, 1934.

Therapy of Nonmalignant Biliary Tract Lesions. Amer. Jour. Digest, Dis. and Nutrition, **2,** 44–46, 1935.

Hyperinsulinism. Nelson's Loose-Leaf Surgery, Vol. 5, Chap. 12, 613–636, 1935.

Adenoma of Islet Cells with Hyperinsulinism. ANNALS OF SURGERY, **101,** 1299–1335, June, 1935. (With Frantz, V. K.)

Opportunities for Graduate Teaching of Surgery in Larger Qualified Hospitals. ANNALS OF SURGERY, **102,** 516–521, October, 1935.

Treatment of Carcinoma of the Ampulla of Vater. ANNALS OF SURGERY, **102,** 763–779, October, 1935. (With Parsons, W. B., and Mullins, C. R.)

Treatment of Carcinoma of the Stomach: Summary of Results. Am. J. Surg., **31,** 246, February, 1936. (With St. John, F. B. and Raiford, T. S.)

Recent Advances in Surgery of the Pancreas. Penn. Med. J., **39,** 473–478, April, 1936. Abstract published in International Surg. Digest, **21,** June, 1936.

Nonulcerative Lesions of the Duodenum. Christopher Textbook of Surgery (revised ed.) Wm. B. Saunders Co., Philadelphia, 1936, pp. 1148–1162.

Silk Technique in the Repair of Clean Wounds. Yearbook of New York & New England Asso. of Railway Surgeons, 1936, p. 49.

Therapy of Chronic Hypoglycemia. Proceedings of Inter-State Post-Graduate Med. Assembly of N. Y., 1934.

Studies in Splenopathy. J. A. M. A., **107,** 1775–1793, November, 1936. (With Thompson, W. P., Brown, D. N., Elliott, R. H. E., and Rousselot, L. M.)

The Combined Spleen Clinic: Results with Medical and Surgical Therapy in Splenopathies. Surg., Gynec. and Obst., **64,** 296–303, February, 1937.

The Clinical Syndrome of Hyperinsulinism. Mass. State Med. J., 1937.

Splenic Vein Pressure in Congestive Splenomegaly. J. Clin. Investig., **16,** 571–572, July, 1937. (With Thompson, W. P., Caughey, J. L., and Rousselot, L. M.)

Surgery of the Pancreas (Revision). Nelson's Loose-Leaf Surgery, Vol. 5, Chap. 8, 397–448B, 1937.

Diseases of the Pancreas (Revision). Cecil Textbook of Medicine, 4th Ed., Wm. B. Saunders Co., Philadelphia, 1937, pp. 818–824.

Surgical Treatment of Tumors of the Pancreas. Pack and Livingston Textbook of Medicine. Paul Hoeber, Inc., 1937.

Acute Intestinal Obstruction. ANNALS OF SURGERY, **107,** 161–197, February, 1938. (With Scudder, J., and Zwemer, R. L.)

Surgical Treatment of Carcinoma of the Ampullary Region and Head of the Pancreas. Am. J. Surg., New Series, **40,** 260–263, April, 1938.

The Surgical Therapy of Hyperinsulinism. J. International de Chirurgie, Bruxelles, 1–35, May-June, 1938.

Surgery of the Biliary Tract (Revision). Nelson's Loose-Leaf Surgery, Vol. 5, Chap. 9, 449–530A, August, 1938.

The Repair of Abdominal Incisions. ANNALS OF SURGERY, **108,** 741–751, October, 1938. (With Elliott, R. H. E., Jr.)

The Medical Surgical Splenopathies, Bull. N. Y. Acad. Med., 2nd Series, **15,** 174–210, **March,** 1939. (With Thompson, W. P., Rousselot, L. M., and Elliott, R. H. E., Jr.)

The Choice and Use of Ligature and Suture Material in the Repair of Clean Wounds. International Abstract of Surgery (Surg., Gynec. & Obst.), **69,** 109–110, August, 1939.

A Consideration of Recent Advances in Medical Science in the Light of Lord Lister's Studies. The Sixth Listerian Oration. Canadian Med. Asso. J., **41,** 323, 1939.

The Essential Principles in Clean Wound Healing. Surg., Gynec. & Obst., **70,** 257–260, February, 1940.

Surgical Treatment of Tumors of the Pancreas. Chap. LXXIV in Pack and Livingston. "The Treatment of Cancer and Allied Diseases." Paul Hoeber, Inc., 1940, pp. 1333–1340.

Diseases of the Pancreas (Revision). Cecil Textbook of Medicine, 5th Ed, Wm. B. Saunders, Philadelphia, 1940, pp. 887–894.

The Use of the Miller-Abbott Tube in the Surgery of the Large Bowel. Surgery, **8,** 289–293, August, 1940.

The Critical Latent or Lag-period in the Healing of Wounds. Presidential Address, American Surgical Association. ANNALS OF SURGERY, **112,** 481–488, October, 1940.

Direct Observations on the Circulation of Blood in Transilluminated Mammalian Spleens. Proc. Soc. Exper. Biol. & Med., **44,** 139–142, 1940. (With MacKenzie, D. W., Jr. and Wintersteiner, M.P.)

End-results of Decompression of the Intestinal Tract with and without Operation. Read at the Bicentennial Celebration, Univ. Pa., September, 1940. Univ. Pa. Bicenten. Conf., May, 1941, pp. 47–56.

Surgery of the Biliary Tract. Bancroft's "Surgical Therapeutics," Vol. I, Sect. 16, pp. 909–941, Appleton-Century Co., 1941.

Recent Studies in the Circulation of the Portal Bed and of the Spleen in Relation to Splenomegaly. The 53rd Mütter Lecture, College of Physicians of Philadelphia, December, 1940. College of Physicians Transactions and Studies, 4th Ser., **8,** 203–217, February, 1941.

Studies in the Microscopic Anatomy and Physiology of the Living Transilluminated Mammalian Spleens. Am. J. Anat., **68,** 397–456, May, 1941. (With MacKenzie, D. W., Jr. and Wintersteiner, M. P.)

Factors Responsible for the Present-Day Low Mortality in Acute Ileus. Northwest Med., **40,** 112–117, 1941.

Observations on the Pathologic Physiology of the Insular and External Secretory Functions on the Human Pancreas. Am. J. Med. Sci., **201,** 629–636, May, 1941. (With Bauman, L., and Hamlin, M.)

Wound Healing. Chapter in "Military Surgical Manual," Vol. 5: "Burns, Shock, Wound Healing and Vascular Injuries." Natl. Res. Council, W. B. Saunders Co., Philadelphia, 1943, pp. 177–194.

The Rationale of Radical Surgery for Cancer of the Pancreas and Ampullary Region. ANNALS OF SURGERY, **114,** 612–615, 1941.

A Consideration of the Surgical Treatment of Tumors of the Pancreas. J. Tenn. State Med. Asso., **35,** 179–189, May, 1942.

Present-day Surgery of the Pancreas. The Bigelow Medal Lecture. New England J. Med., **226,** 513–526, March, 1942.

Nonulcerative Lesions of the Duodenum (Revision). Christopher's Textbook of Surgery (3rd Ed.), Wm. B. Saunders Co., Philadelphia, 1942, pp. 1130–1144.

The Rôle of the Liver in Surgery. N. Y. State J. Med., **43,** 53–56, January, 1943.

A Study of the Results of the Examinations in Anatomy by the American Board of Surgery. J. Asso. Am. Med. Coll., May, 1943.

Basic Principles in the Treatment of Thermal Burns. ANNALS OF SURGERY, **118,** 187–192, August, 1943.

Surgery of the Terminal Ileum, Cecum, and Right Colon. Surgery, **14,** 321–327, September, 1943.

Diseases of the Pancreas (Revision). Cecil Textbook of Medicine, 6th Ed., Wm. B. Saunders, Philadelphia, 1943, pp. 791–798.

The Diagnostic Value of Pancreatic Function Tests in 47 Surgically Treated Cases. Am. J. Med. Sci., **207**, 281–290, March, 1944. (With Bauman, L.)

Hyperinsulinism in Relation to Pancreatic Tumors. The Trimble Lecture. Surgery, **16**, 289–305, August, 1944.

Recent Advances in the Treatment of Wounds. Proc. Am. Philosophical Soc., **88**, 177–181, September, 1944.

The Problem of Postwar Surgical Training for Returning Medical Officers. New England J. Med., **231**, 405–407, September, 1944.

Pancreaticoduodenectomy for Islet Carcinoma: A Five-year Follow-up. ANNALS OF SURGERY, **121**, 847–852, June, 1945.

The Problem of Portal Hypertension in Relation to the Hepatosplenopathies. ANNALS OF SURGERY, **122**, 449–475, October, 1945.

Surgery of the Pancreas (Revision). Nelson's Loose-Leaf Surgery, Vol. 5, Chap. 8, 1945, pp. 397–421.

Diseases of the Pancreas. Nelson's Loose-Leaf Medicine, 1945.

The Rationale of Portacaval Anastomosis. N. Y. Acad. Med. Bull. (In press.)

Observations on Radical Surgery for Lesions of the Pancreas. Surg., Gynec. & Obst. (In press.)

PAPERS NOT PUBLISHED

Hepatosplenopathies from Standpoint of Surgical Therapy. Read at School of Tropical Medicine, Puerto Rico, 1933.

Studies from the Spleen Clinic of the Vanderbilt Clinic and Presbyterian Hospital. Read at Youngstown, Ohio, 1936.

The Splenopathies Amenable to Surgical Therapy. The Hodgen Lecture. Read at meeting of St. Louis Medical Society, 1938.

Indications for and Results of Operations upon the Spleen. Read at Rochester, N. Y. Academy of Medicine, 1939.

An Evaluation of Certain Laboratory Blood Studies in Relation to the Surgical Patient. Read at the Albany Medical College, 1939.

The Diagnostic and Therapeutic Aspects of Pancreatic Adenoma. Read at meeting of Chicago Surgical Society, 1940.

The Application of Chemistry to Certain Problems in the Pre- and Postoperative Care of Surgical Patients. Read at Kansas City Academy of Medicine, 1940.

The Criteria for Splenectomy in the Splenopathies. Read at meeting of the American Medical Association, 1940.

Surgery of the Pancreas. Read at meeting of the American College of Surgeons, 1940.

Indications for and Results Following Splenectomy. Read at Duke University Symposium, 1940.

A Discussion of Certain Splenopathies in Relation to the Vascular Bed of the Spleen. Read at the Evans Memorial Hospital, Boston, March, 1941, and at meeting of the Hartford Medical Society, April, 1941.

Recent Advances in Surgery of the Pancreas. Read at meeting of the Society of Bellevue Hospital Alumni, October 1, 1941.

Experimental Data in the Study of the Pathogenesis of Certain of the Splenopathies. Read at Mayo Foundation, October, 1941.

Recent Developments in Surgery of Pancreatic Tumors. Read before Nassau County Surgical Society, May, 1943.

A Rationale for the Therapy of Portal Hypertension. The Walter L. Niles Memorial Lectureship. Read at Cornell Univ. Med. College, 1946, and at Alpha Omega Alpha meeting, Yale, 1946.

NONSURGICAL BIBLIOGRAPHY

Opportunities for Graduate Teaching of Surgery in Larger Qualified Hospitals. ANNALS OF SURGERY, **102,** 516–521, October, 1935.

Rôle of the Nestorians as the Connecting Link between Greek and Arabic Medicine. Annals Med. Hist., **8,** 313–323, July, 1936. Also Bull. N. Y. Acad. Med., 2nd Series, **12,** 446–462, 1936.

The Medical School and Hospital of Gondi-Sapor and Its Influence on Arabian Medicine. Proc. Charaka Club, **9,** 95–110, 1938.

A Visit to the Vatican Library. Read at meeting of the Charaka Club, April, 1941.

Lukens Surgical Sutures

Heat-sterilized and sealed in an iodine storing solution, the IODIZED gives a double assurance of sterility. Our Io-Chrome tanning imparts an ideal resistance to absorption.

This excellent *non*-iodized suture possesses a fortunate combination of pliability and strength. Like the IODIZED, it is USP, and is prepared in the Plain and Chromic durations.

Dulox Needles . . . swaged onto Catgut, Silk and Linen . . . are available in a wide variety of single and double combinations for all procedures in general and specialized surgery.

Sterile and "ready for use" direct from our special tube-containers, Lukens BONEWAX (Horsley's method) is conveniently and safely applied, assisting in perfect hemostasis.

Also: BOILABLE SURGICAL GUT· LIGATING REELS • SILKS • LINENS AND SPECIALTIES. *Samples on request.*

Unusual strength permits the use of fine sizes

C. DeWITT LUKENS CO., *St. Louis, Mo.*

SINCE 1904...MANUFACTURERS OF QUALITY SUTURES EXCLUSIVELY

EXPERIENCE WITH CURARE IN ANESTHESIA

VIRGINIA APGAR, M.D.
NEW YORK, N. Y.

THE USE OF CURARE as a supplement to anesthesia has gained a remarkable following since its introduction into medical practice in 1938. After the pioneer work of Gill,[1] and the use of the drug initially by neurologists and psychiatrists, Griffith,[2] at the suggestion of Wright, first used curare in patients during anesthesia to produce skeletal muscle relaxation and reported his results in 1942. Since that date, several hundred papers have appeared which are almost unanimous in acclamation of the drug. Almost no ill effects of the drug other than respiratory depression have been reported. It has been pointed out repeatedly that the use of curare to produce relaxation is no substitute for good anesthesia, with ample oxygenation and efficient removal of carbon dioxide. The importance of its administration by a physician who is aware of the need of immediate assisted respiration and is able to perform it promptly and adequately has been properly stressed.

Many questions remain to be answered, both in the laboratory and in the clinic. There is some disagreement as to the tone of the intestines following a dose of curare, and the proper treatment of the change in tone, if such is observed. There is some doubt whether a pharmacologic antidote, such a prostigmine, is needed in addition to the physiologic antidote-artificial respiration. Whether it is wise to use the drug in the presence of shock and hemorrhage is not known. It is possible that the postoperative incidence of atelectasis and pneumonia will not be decreased as much as expected because of the time necessary for complete recovery of the intercostal muscles and diaphragm. Many more clinical reports are needed to clarify this point. The signs of anesthesia, both with inhalation and intravenous drugs must be redescribed. It is exceedingly difficult to be certain of the state of unconsciousness when the action of all skeletal muscles has been depressed and the patient's trachea has been intubated as well. This fact has been made vivid to us by the observation of a patient, himself a surgeon, undergoing a lobectomy for bronchiestasis.[3] Anesthesia was induced with pentothal and curare, an endotracheal tube was inserted and the operation begun, with pentothal and curare added at intervals. Objectively, the anesthesia was highly successful, but the patient remembers vividly every detail of the last half of the operation, and was unable to communicate his discomfort to the anesthetist. Another question to be answered is that of the advisability of early ambulation in patients who have received curare in generous doses. Experience with a few unanesthetized patients who have been curarized to the point of marked respiratory depression, and then allowed to walk after one or two hours, with resulting severe muscle pains, suggests that ambulation on the day of anesthesia is inadvisable.

This report of 200 consecutive cases which received curare during anesthesia, since November, 1943, will answer none of the above questions but will

describe our experience with the drug in a teaching clinic. In all cases the anesthesia was administered by physician anesthetists after at least three months of an active residency. No one was allowed to use the drug unless he demonstrated a good working knowledge of the signs of anesthesia. He also must have demonstrated his ability to introduce an endotracheal tube under direct vision with rapidity and lack of trauma. The decision as to the selection of this drug for use in a certain patient was made in consultation with a senior anesthetist, but the dose and management of the complications were left to the resident. The drug used was "Intocostrin," marketed by E. R. Squibb and Sons, in a 2% concentration. The drug was usually stored in the refrigerator. The intravenous route was the only one employed. While a vein in the forearm or hand was the usual site chosen, the external jugular vein was frequently used. Introduced into infusion tubing near the needle, this solution was found to mix freely with saline, glucose or blood, but to form a precipitate with all pentothal concentrations. The rate of injection was rapid. The maximum action was almost always present in 60 seconds, while the duration of action varied greatly with the anesthetic agent, the plane of anesthesia when the drug was administered and the length of time that plane had been established.

Twenty different physicians administered curare in these 200 patients. The region of operation is listed in Table I.

TABLE I

Region	Cases
Upper abdomen	95
Lower abdomen	42
Chest, intrapleural	18
Chest, extrapleural	1
Head and neck	39
Rectum and prostate	4
Extremity	1

The anesthetic agents used are listed in Table II.

TABLE II

Agent	Cases	No. Intubated
Ether	127	81
Pentothal	42	31
Cyclopropane	24	12
Spinal/N_2O	2	0
Avertin/N_2O	3	0
Spinal/pentothal	1	0
Procaine infiltration	1	1
		125

The principal reason for its use, as given by the anesthetist, is listed in Table III.

TABLE III

Relaxation of the surgical field	127
Aid to intubation	56
To facilitate induction	8
To decrease respiratory movements	4
To control excitement during induction	1
To use less anesthetic agent	1
For demonstration purposes	1

The dosage and anesthesia time are given in Table IV.

TABLE IV

	Average Initial Dose	Average Total Dose	Average Anes. Time
Ether	42 mg.	52.3 mg.	153 mins.
Pentothal	82 mg.	91.5 mg.	50 mins.
Cyclopropane	42 mg.	77.7 mg.	140 mins.

TABLE V

RESPIRATORY EFFECTS OF CURARE

	No Effect	Slight Depression	Moderate Depression	Marked Depression	Apnea
Ether (2, no data)	69 (55%)	4	23	14	15
Pentothal (1, no data)	33 (80%)	1	2	1	4
Cyclopropane (2, no data)	12 (55%)	2	1	0	7

In no case with ether or pentothal anesthesia, was the apnea planned. With cyclopropane, controlled respiration had been chosen as the method of choice in several cases, so that the apnea may not have been a result of overdosage of the drug, but rather, the result of technic used.

TABLE VI

CIRCULATORY EFFECTS OF CURARE

	No Effect	Rise in Systolic	Fall in Systolic	Rise in Pulse	Fall in Pulse	Remarks
Ether (1, no data)	93 (73%)	12	10	5	1	1 arrhyth. 1 variable
Pentothal (2, no data)	35 (87%)	0	1	2	2	
Cyclopropane (1, no data)	20 (87%)	1	1	1	0	

The anesthesia records kept during pentothal and curare anesthesia are not as accurate as those with ether or cyclopropane, for seldom were two anesthetists available, the operations were usually performed in the dark and the anesthetist was unusually busy. We feel that never is a record more important than the welfare of the patient.

TABLE VII

RETURN OF REFLEXES AT END OF OPERATION

	Reflexes Back	Airway Left In	No Data	Dead
Ether	71 (60%)	46	9	1
Pentothal	29 (83%)	6	7	
Cyclopropane	17 (80%)	4	3	

OTHER COMPLICATIONS DURING OPERATION

Hiccoughs	3
Profuse diaphoresis	3
Profuse secretions	10
Death from hemorrhage	1
Death during resuscitation following overdosage	1

This last case deserves further description. A four-day-old female was admitted with deep jaundice and intestinal obstruction. Temp. 99° F., hemoglobin 21.8 Gm.; R. B. C. 5,620,000; W. B. C. 8,550. Rh negative; Wt. 2230 grams (4.9 lbs.) An infusion, and transfusion were given, a stomach tube was inserted, and a diagnosis of atresia of the jejunum was made and corroborated at operation, where a 10 cm. obstruction was found. An end-to-side jejunojejunostomy was performed. Because of the obviously poor risk of the patient, it was thought that curare might be ideal to quiet respiration enough to allow a satisfactory surgical field. No premedication was used. A few cubic centimeters of 1 per cent procaine hydrochloride was used for the skin incision. Ten milligrams of curare was the dose selected, and was given intravenously. Even during the administration, some respiratory depression was noted, but the full dose was given. Apnea ensued immediately. There was some difficulty in finding an endotracheal tube small enough for the larynx, so that pharyngeal oxygen insufflation was begun, with manual pressure on the chest. Finally, a woven cotton suction catheter was cut to a 3-cm. length and inserted into the trachea, and after suction, a gentle insufflation of oxygen was begun through a Y-tube. Observation and palpation of the chest showed that the lungs could be inflated easily by this method. However, oxygenation became poorer, in spite of a flow of only 100 cc. of oxygen per minute. It was felt that the lumen of the tube was too small to permit good exhalation, and there was not enough leakage around the tube even with manual assistance on the chest. The pulse rate fell from an initial 140 to 80, indicating a severe hypoxia. The endotracheal tube was removed, and a small face mask with bag attached, was substituted. A to-and-fro infant's canister was used for a few minutes, but the leakage around the stomach tube indicated that it was not necessary to plan for carbon dioxide absorption. Oxygenation improved markedly with gentle, intermittent pressure on the bag. The pulse rate rose to 120, where it remained for the next two hours and a half.

The operation was completed in 45 minutes. Three other attempts were made to return to an endotracheal air-way, but in each instance the condition of the infant was better with mask and bag inflation. To prevent overdistention of the stomach, the stomach tube was aspirated continuously. One hour and 50 minutes after administration of the curare, very slight contraction of the mylohyoid muscles could be felt. No diaphragmatic action at all could be seen, and no ventilation was produced by the contractions. After another 30 minutes, with no further improvement, a trickle of 100 per cent carbon dioxide was held near the face for a few seconds, without any result or change in condition. Ten minutes later, 0.120 mg. of prostigmine was administered intramuscularly, with no noticeable effect during the next 20 minutes. At this time, a medical student suggested rectal dilatation as a respiratory stimulus. We were surprised to find that the diaphragm contracted sharply and vigorously, but without producing any ventilation, for the vocal cords were tightly adducted during the stimulus. The patient was reintubated, and the stimulus continued. Irregular diaphragmatic movements continued, but the heart, which seemed

unaffected as long as the patient was well oxygenated, slowed down abruptly when rectal dilation was started, and failed during the next 30 minutes.

Autopsy revealed no other findings except bilateral bronchopneumonia, which had been present about two days. A sample of brain tissue was sent to the Toxologic Laboratory at Bellevue Hospital, which reported a content of 0.25 mg. of curare per 200 mg. of brain tissue.[4] We are at a loss to know how to interpret this result. It was not until many hours later that it was discovered from the chart that 1 cc., or 20 mg., had been administered instead of the 10 mg. planned.

POSTOPERATIVE COMPLICATIONS

There were 13 deaths in addition to the two in the operating room. Six of these were following esophagectomy. Since the operative time averaged seven hours, and the doses of curare had been small, it was felt that they were unrelated to the use of the drug. Three deaths occurred after two weeks and are unrelated. One man died on the first day following suture of a perforated jejunum, and was found to have a fulminating peritonitis at autopsy. Another man of 70, following gastrectomy for carcinoma, developed a mild bronchopneumonia for two days, but was improved the next two days. He died suddenly at night on the fourth day. No autopsy was obtained, and his death remains unexplained. The 12th death occurred in a man, age 45, who had a previous laryngectomy for carcinoma. He developed a severe intestinal obstruction, with accompanying shock. Operation revealed no definite pathologic lesion. He was awake at the end of the operation, which lasted 110 minutes, and died three days later, still undiagnosed. The death of the 13th patient also remains unexplained. A 250-lb. man in good health underwent a ventral incisional herniorrhaphy with nitrous oxide-ether anesthesia. Seven point eight grams of avertin were given him for basal narcosis in addition to 12 mg. morphine and 0.0005 Gm. scopolamine six minutes before anesthesia, subcutaneously. This dose did not depress him unduly, and two hours later, 60 mg. curare was given because abdominal relaxation was not adequate. Moderate respiratory depression resulted but was easily treated because an endotracheal tube was in place. Ventilation was normal for the next 75 minutes. Circulation was excellent throughout the operation. His pharyngeal reflexes had returned at the end of a 355-min. procedure. Ten minutes after return to bed, he was found dead. Roentgenograms of the chest at this time showed normal lung fields. No autopsy was obtained. It is probable that respiratory obstruction was the cause of death.

In addition to the pulmonary complications mentioned above, there were two cases of atelectasis, and two of bronchopneumonia, all of which responded readily to treatment. The incidence of other complications, such as vomiting, urinary retention, headache, and cough was at least as low as in similar types of operations anesthetized without curare, and seemed lower.

Discussion.—The results obtained in the 25 tonsillectomies anesthetized with pentothal and curare were appreciably better than a parallel series of 25

cases without curare. The recovery in the group without curare was prolonged and marked by extreme restlessness, necessitating much more nursing care than is available on a nose and throat ward. With the use of curare, much less drug was used, and the patients were awake shortly after completion of the operation. It is imperative to perform a thorough topical spray of the pharynx before intubation with pentothal especially, and advisable when the combination of drugs is used. Two per cent butyn sulphate gave satisfactory results, although 4 per cent cocaine was used in a few cases. All tonsillectomy patients, in the adult group, are intubated.

Our experience with prostigmine has been too small for comment. Only three patients received the drug, in 0.5-mg. doses, and no effect was observed in any of the three. Either the dose was too conservative or the drug ineffective through age. We have felt that assisted respiration is much more important than drug therapy.

The main disadvantage to the use of curare, as we have observed it in this clinic, is the difficulty in teaching signs of anesthesia. Even without curare, the signs are often subtle enough. The demand for the drug during upper abdominal cases is increasing to such an extent that it may not be necessary to teach third and fourth planes of anesthesia. From the accumulating literature, it is becoming evident that there is minimal metabolic disturbance following the use of the drug, which justifies its use in such patients. A reëvaluation of the signs of anesthesia is in order. Curare, we feel, has already assumed a permanent place as a supplement to anesthesia, and as more experience is gained, even respiratory depression may be obviated to a large extent.

SUMMARY

1. A series of 200 anesthesias supplemented by curare is presented.

2. One death was related to the use of curare, and was due to accidental overdosage, and too vigorous resuscitation. It is suggested that the concentration of the drug be changed to 1 per cent (1 cc. = 10 mg.) to lessen the hazard of mathematical errors.

3. There were no complications in the postoperative period related to the use of the drug.

REFERENCES

[1] Gill, R.: White Water and Black Magic. New York. Henry Holt and Co., 1940.
[2] Griffith, H. R., and Johnson, G. E.: Anesthesiology 3: 418, July, 1942.
[3] Bolger, T.: Personal Communication, 1945.
[4] Gettler, A. O.: Personal Communication, 1945.

THIOURACIL IN THE TREATMENT OF THYROTOXICOSIS

EXPERIENCE OF THE THYROID CLINIC OF THE COLUMBIA-PRESBYTERIAN MEDICAL CENTER

HENRY ARANOW, JR., M.D., ROBERT H. E. ELLIOTT, JR., M.D., VIRGINIA KNEELAND FRANTZ, M.D., GEORGE W. MELCHER, JR., M.D., AND SIDNEY C. WERNER, M.D.

NEW YORK, N. Y.

FROM THE DEPARTMENTS OF MEDICINE AND SURGERY, PRESBYTERIAN HOSPITAL, NEW YORK, N. Y.

IN 1925, shortly after the widespread use of iodine revolutionized the treatment of thyrotoxicosis,[8] the Thyroid Clinic of the Presbyterian Hospital was organized by two internists, Drs. W. W. Palmer and B. J. Sanger, and a surgeon, Dr. W. B. Parsons, Jr. Subsequently other members of the staff joined the group which eventually included several surgeons and internists, a surgical pathologist, a psychiatrist and an ophthalmologist. An effective follow-up system* made it possible to observe long-term results of various therapeutic approaches, and wherever possible the patient was followed by the attending physician or surgeon who directed the therapy. Some patients have been under observation for more than 20 years.

The publication of Astwood's[2] now classical paper in May, 1943, marked the advent of a new principle in the treatment of human thyroid hyperfunction; a multitude of reports have since confirmed his results,[5, 6, 9, 11, 14] It was felt that the Thyroid Clinic, with the data accumulated over years of iodine, surgical and radiotherapeutic control of hyperthyroidism would provide a proving ground for comparison of the new agent with older treatments. It is greatly regretted that Drs. W. B. Parsons Jr. and Lawrence Sloan, the senior surgeons, who were serving with the Armed Forces, were not present during the greater part of this study.

The administration of thiouracil† to patients with thyrotoxicosis was begun in August, 1943. Not all cases seen in the Thyroid Clinic were treated with this drug; most of the cases with toxic nodular goiter, and a considerable number of primary cases, were still prepared for operation with iodine. Economic and geographic considerations sometimes also made iodine and surgery the treatment of choice. The patients who received thiouracil therapy were, however, an unselected group.

* Acknowledgment is hereby made to Miss Retta Pinney, R.N., without whose untiring interest and effort this follow-up could not have been accomplished.

† The thiouracil used in these studies was supplied through the courtesy of Doctors B. W. Carey and Stanton M. Hardy, of the Lederle Laboratories.

The problem seemed to divide itself naturally into four parts, each the primary interest of one of the authors, and so discussed here: (1) Primary toxic goiter—thiouracil treated. (2) Recurrent toxic goiter—thiouracil treated. (3) Thyroidectomy following thiouracil therapy. (4) Pathology.

PRIMARY TOXIC GOITER

(*77 Cases*)

The 77 patients who comprise this group were seen either on the wards of the Presbyterian Hospital, or were referred from the general Medical and Surgical Out-patient Department to the Thyroid Clinic. In addition to complete histories, physical examinations and routine laboratory studies, the work-up included blood counts, basal metabolic rate determinations, estimations of the fasting serum cholesterol, chest roentgenograms, and, when indicated, electrocardiograms. Thirty-four of the cases were hospitalized before thiouracil therapy was begun; the remainder were treated as out-patients. The series included 59 females and 18 males; there were 57 white, 18 colored, and two Chinese patients. Their ages ranged from ten to 72 years, the majority being in the fourth and fifth decades. Of the 77 cases, 73 had toxic diffuse goiter, three had toxic nodular glands, and there was one case of acromegaly with hyperthyroidism.

Thiouracil was given to each patient in an amount sufficient to last only until the next appointment. Toxic reactions were described in detail to the patient with instructions to stop the drug at once, and come to the Clinic should any suspicious symptoms appear. The drug was administered in divided doses, but no more than three doses per day were given to ambulatory patients, and no particular effort was made to have the intervals precisely equal. Our earliest cases were treated with 1.2 Gm. per day, but when it became apparent that 0.6 Gm. was equally effective, initial dosage was reduced to this level. Fifty-seven patients started with 0.2 Gm. three times a day. On most of this group white blood and differential counts were performed weekly, for the first eight weeks, then bimonthly for the next eight weeks, and at longer intervals thereafter. The results of the blood examinations were known to the examiner before the next week's program was determined. At the beginning of the study, frequent measurements of basal metabolic rate and serum cholesterol were made, but as the pattern of response became more familiar such frequent checks were no longer necessary.

The patients were urged to eat a well-balanced, high vitamin, high caloric diet, but no vitamin supplements, calcium, or other adjuvant nutritional factors were routinely administered. The great majority received no phenobarbital or other sedative medication.

Thyrotoxicosis was controlled in every case where thiouracil therapy was not prematurely discontinued. In general, the metabolic response, improvement in symptomatology, and the disappearance of evidences of thyroid hyperfunction was similar to that reported by other authors. The over-all results will be presented, with emphasis only on features of particular interest.

Subtotal thyroidectomy was performed on 39 patients and they will be considered later. It is noteworthy that 12 of the cases operated upon had been taking thiouracil for over 14 weeks. Most of these were originally treated in the hope of obtaining a permanent remission without surgical therapy, but requested thyroidectomy because of the uncertainty of the outcome with thiouracil alone and because of the trouble and loss of time involved in repeated Clinic visits, blood counts, basal metabolic rate determinations, *etc.*

Seven patients have been lost to follow-up. In each case, Clinic attendance was faithful until the evidences of hyperthyroidism had disappeared; after that, even with letter or social service inquiry, they failed to return.

In 14 patients thiouracil was deliberately discontinued.[3, 14] This was not done until the basal metabolic rate had been held within normal limits for six months or more, and the maintenance dosage before the withdrawal was 0.2 Gm. per day, or less.[3] One of this group was asymptomatic for over a year, and then had a recurrence which was treated, at his request, with iodine alone and surgery.* Four had a return of hyperthyroidism within six months. One of these was the patient with acromegaly. All the recurrences were readily controlled again with thiouracil.

Eight patients have been asymptomatic, six of these from one to two years, two from six months to a year. One other patient has been off the drug for two months only—too short a period to warrant any conclusion. Seven of these nine patients had moderately enlarged glands before therapy and some degree of enlargement persists.

The only death in the series was due to a primary carcinoma of the liver which occurred in a 38-year-old Chinese male. He died 18 months after the administration of thiouracil was started and seven months after the appearance of symptoms of carcinoma.

Treatment continues in 21 cases. One of these requires a maintenance dosage of 0.4 Gm. per day, 18 months after starting therapy.

The toxic reactions which occurred in this group have been included in the two large studies which have recently been published.[7, 12] They are briefly summarized here, and some noteworthy aspects reviewed. In ten instances these idiosyncrasies have been severe enough to make permanent interruption of thiouracil therapy necessary. In five cases, routine blood examinations revealed dangerous granulocytopenia in asymptomatic patients. The drug was immediately withdrawn in all. Four patients never became ill, and their blood counts returned promptly to normal. The fifth developed absolute agranulocytosis four days after the initial count, and later had angina. She made an uneventful recovery. The earliest reaction occurred three weeks after the administration of 0.6 Gm. each day, and the latest followed after 18 months of uneventful treatment, with numerous normal blood counts. In this instance, on a maintenance dose of 0.3 Gm. o.d. the count revealed only 15 per cent neutrophiles in a total of 1,750 white cells.

* This case, therefore, does not appear in Table III.

Five patients had miscellaneous early reactions, such as fever, rash, thyroiditis, *etc.*, which have been described in the articles cited. Each idiosyncrasy of this type was checked by the readministration of a pilot dose of the drug, with a return of the particular toxic reaction.

In four instances white blood counts below 3,500 were disregarded since they did not differ significantly from the patient's usual values. There were no untoward findings following continued treatment.

The results of thiouracil therapy have ranged from the extremely dramatic, with a fall of 40 per cent in basal metabolic rate and a 28 per cent increase in body weight in three weeks, to the quite unimpressive, when 11 months of therapy with a dosage of 0.6 Gm. daily still permitted mild thyrotoxic symptoms and a basal metabolic rate of plus 20 per cent. In this patient, another month of therapy without change in dosage reduced his basal metabolic rate to plus 6 per cent and freed him of all symptoms.

Ophthalmologic studies were carried out on most of these patients by Drs. Russell Nicholl and Noel F. Stow. These will be reported in detail in another publication. No dangerous progression of exophthalmos occurred with thiouracil treatment in this primary group.

RECURRENT TOXIC GOITER
(*30 Cases*)

It was recognized early after the introduction of thiouracil that the danger of agranulocytosis might limit prolonged treatment with the drug to those categories of cases where surgery with or without roentgenotherapy had failed or was inadvisable. A separate study was, therefore, made of a group of recurrent cases. The results of treatment for the past two and one-half years are reported here.

Thirty cases of recurrent toxic goiter have been followed. Five of these, four women and one man, were deemed suitable for operation, were prepared with thiouracil, and are discussed in the sections on surgery and pathology. Of the remaining 25 cases six were men and 19 were women. Ages ranged from 22 to 56 years.

In 23 cases the results of treatment were observed for considerable periods of time, *i.e.*, 18 for 2—2.5 years; three for 1.5—2 years; two for 9 months—1.5 years. In two others therapy was discontinued. One of these died on the 11th day after contracting agranulocytic angina, although showing evidence of recovery in the white cells, because of thrombosis of the internal carotid artery. One developed drug fever and could not be treated further, although followed in the Clinic. One of the women developed a carcinoma of the cervix during treatment.

White blood and differential counts were done at two-week intervals throughout the study. Basal metabolic rate and fasting cholesterol determinations were done on the same day as the blood counts early in the study, later every one or two months.

Dosage.—An initial dosage of thiouracil 0.2 Gm. three times a day was

used in all cases, but in several instances 0.4 Gm. three times a day was needed to reduce the metabolic rate. No failure to restore the basal rate to normal was encountered. Maintenance dosage of the drug varied from 0.1 to 0.6 Gm. a day, in divided amounts. Escape from a maintenance dosage that had been previously sufficient occurred eight times, as late as 14 months after the start of treatment. An increase in the dose readily controlled these latter.

Toxicity.—The toxic responses have been incorporated with a larger series discussed elsewhere.[7, 12] Agranulocytosis occurred four times in three patients, as late as eight months after starting treatment. One drug fever and eight leukopenias were enough to warrant interrupting the administration of the drug. Renewed treatment lowered the white count a second time in only one patient.

Fasting Cholesterol.—This determination was useful in estimating the response to thiouracil in the early stages of treatment, tending to rise above 300 mg. per cent. In the later period the basal rate appeared to reflect changes in thyroid function better than the cholesterol level.

Exophthalmos.—A significant progression of exophthalmos was noted only once, a 5 mm. advance in one eye to equal the exophthalmos in the other eye. This occurred during two years of treatment.

Remissions on Stopping Treatment.—The results of stopping therapy are discouraging. Treatment was discontinued 24 times in 19 patients (Table I). Remissions for a year were encountered in two patients, one after four months and the other after 1.5 years of treatment. A third patient showed borderline thyroid toxicity one year after discontinuing the drug, and is very probably reactivated. A fourth patient had a year of therapy and has been symptom-free for five months. The other 15 patients showed recurrence of thyrotoxicosis within from one to six months after discontinuance of treatment, most of them by the third month (Table II). In seven of these in which overactivity recurred, the drug was not discontinued until after one to two years of treatment. Thiouracil therapy controlled the overactivity on reinstitution in all instances.

TABLE I

SHOWING MONTHS AFTER STARTING TREATMENT AT WHICH THERAPY WAS DISCONTINUED

(Basal metabolic rates were normal throughout after the induction period of from 2 to 6 weeks)

Months	Number of Cases
0– 3	1
3– 6	6
6–12	10
12–18	4
18–24	1
24 or more	2

THYROIDECTOMY

(*47 Cases*)

Forty-four cases were referred for operation between October, 1943 and January, 1946, and three were managed directly, making a total of 47. Of the

FIG. 3

FIG. 4

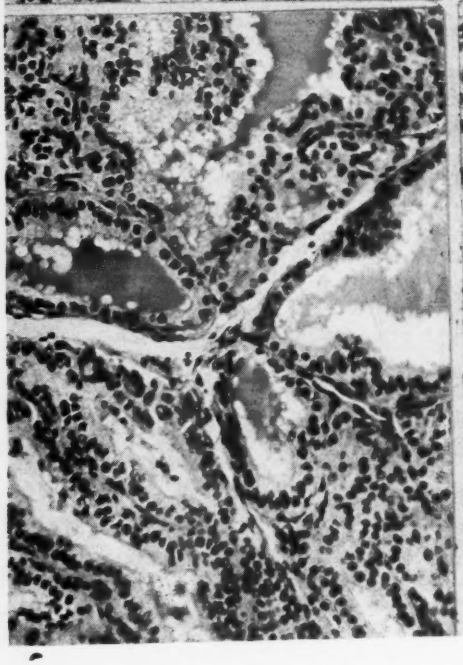


FIG. 1

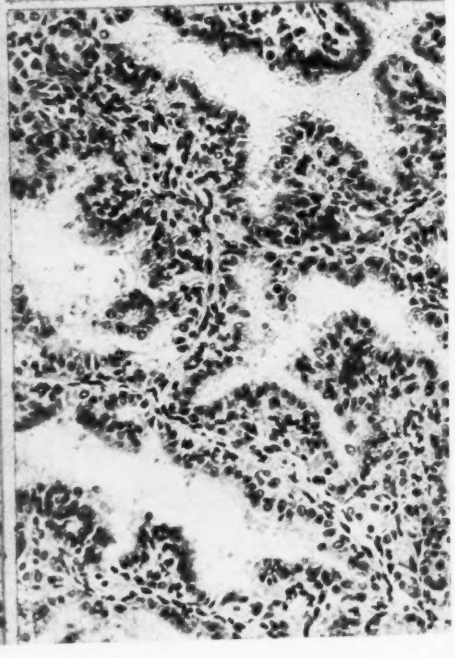


FIG. 2

TABLE II

SHOWING MONTHS AT WHICH RECURRENCE OCCURRED AFTER DISCONTINUANCE OF THERAPY

Months	Number of Cases
1	8
2	7
3	2
4	0
5	1
6	1

toxic diffuse glands, as will be seen from Table III*, 18 cases were prepared by thiouracil alone, six had iodine preceding thiouracil therapy, but, in essence, should be regarded as prepared with thiouracil, 14 had thiouracil supplemented with preoperative iodine, and four were recurrent toxic diffuse goiters. There were in addition five nodular goiters of which one was also a recurrence. It will be seen from the table that the preparation was variable, either because there were contraindications to the continuance of the drug, or because of the laborious nature of continued drug therapy. Where discontinuance was necessitated because of toxic reactions, the preparation for operation was not always adequate. When it was adequate the basal metabolic rate had returned to normal, symptoms had abated, and the pulse and weight gain were satisfactory. The introduction of iodine as an adjuvant is recent,[5, 10] and not as yet uniform, but the present plan is to give iodine for two weeks prior to operation and to discontinue thiouracil one week before the procedure.

Operative Findings.†—Unusual difficulty with hemostasis and unusual friability of the gland were encountered in some of these cases. It is impossible to assay this accurately, particularly when several surgeons, some less experienced than others—as in the case of the resident staff—are reporting their findings. The preoperative use of iodine has probably lessened the exces-

FIG. 4

FIG. 2

FIG. 1.—S. P. 86068. Moderate Thyrotoxicosis. Iodine 16 days. Considerable colloid. Marginal vacuolization. Papillary infolding.

FIG. 2.—S. P. 84810. Moderate Thyrotoxicosis. Iodine 16 days. Marked hyperplasia. Papillary infoldings. Fragmentation and disappearance of colloid.

FIG. 3.—S. P. 88452. Severe Thyrotoxicosis. Thiouracil 23 weeks. Diffuse extreme hyperplasia. "Classic" response. Compare with Fig. 4—28 weeks.

FIG. 4.—S. P. 93201. Severe Thyrotoxicosis. Thiouracil 28 weeks. Patchy moderate hyperplasia. Moderate late involutional changes. Compare with Fig. 3—23 weeks.

* This table has been deliberately modeled after Table I in the article by Moore, *et al.*, so that the two groups of cases could be compared.

† A number of these cases were under the care of Doctor J. M. Hanford who was the senior surgeon in the Clinic during the war years.

FIG. 7

FIG. 8

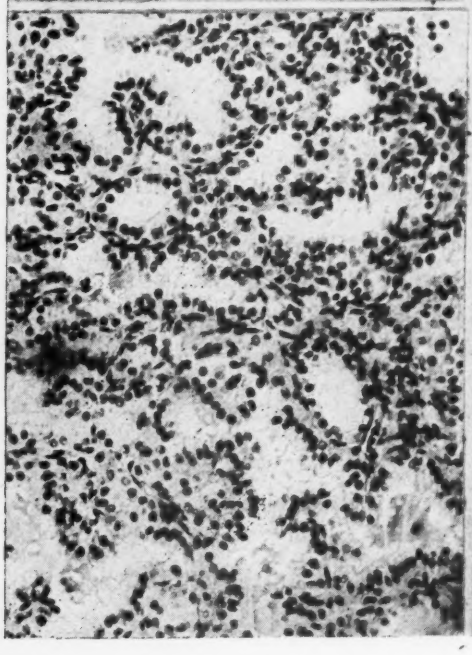


FIG. 5

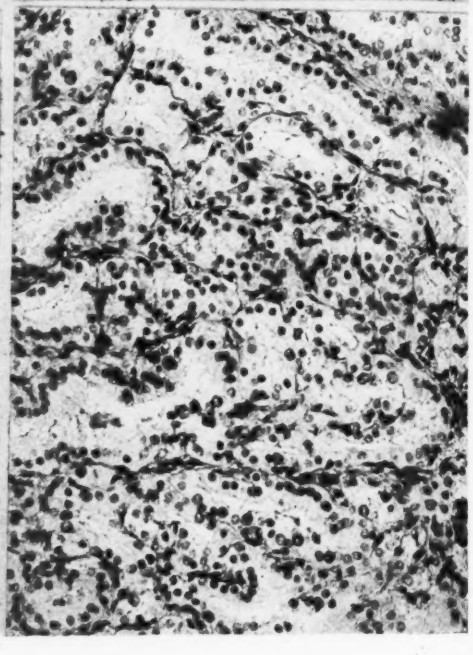


FIG. 6

sive bleeding, although it is not possible to establish this point in so small a series. In the five nodular glands removed these technical difficulties did not arise.

Postoperative Course.—This was in general smooth, without thyrotoxic reaction. Full-blown "storm" is seldom a controversial finding, but the interpretation of lesser degrees of postoperative reaction is obviously often a matter of individual opinion. In ten of these 47 cases there were toxic reactions of varying severity. In seven of these cases this can probably be attributed to inadequate anteoperative preparation as described above. In one case in which a temperature rise to 105° F. developed the day following operation, considerable difficulty had been experienced in introducing an intratracheal tube during anesthesia. In spite of the height of the fever there was no concomnitant evidence of "storm." The reaction was attributed to the onset of an acute upper respiratory infection and an ulcerative tracheitis. The remaining two cases, however, seemed to be well prepared for operation and yet one, with no previous history of cardiac difficulties, developed paroxysmal fibrillation on the first postoperative day, and the patient appeared definitely thyrotoxic. The other had a temperature rise to 103° F. within 24 hours, and also appeared quite toxic. The course was, in general, no different from the average severe case of thyrotoxicosis prepared on iodine alone. Moreover, this case had received iodine as an adjuvant measure for two weeks prior to operation which was not so in the other toxic case. It will be seen from the chart that there were three postoperative hemorrhages, whereas in the control 30 iodine-prepared cases, there was only one. In two of the three thiouracil cases the hemorrhage was not because of uncontrollable ooze but because of failure to ligate a major vessel—a definite technical error.

PATHOLOGIC STUDIES

In an effort to correlate the gross and microscopic findings with the changes thought to be induced by the administration of thiouracil, 42 of the 47 surgical specimens were selected for study. The five nodular glands were omitted

FIG. 8

FIG. 6

FIG. 5.—S. P. 80248. Moderate Thyrotoxicosis—Recurrent. Iodine 7 days.
Compare with Fig. 6 from the same patient 3 years later. Diffuse extreme hyperplasia.

FIG. 6.—S. P. 91490. Moderate Thyrotoxicosis—Recurrent. Thiouracil 7 weeks.
Compare with Fig. 5 from the same patient, 3 years earlier. Patchy extreme hyperplasia.

FIG. 7.—S. P. 93121. Moderate Thyrotoxicosis. Thiouracil 10 weeks and iodine 10 days.
Patchy slight hyperplasia. Diffuse late involution. Lymphoid follicles.

FIG. 8.—S. P. 92512. Moderate Thyrotoxicosis. Thiouracil 52 weeks.
Moderate hyperplasia. Early involution.

because of the small number and the variable pathologic picture. The specimens studied are included in the table in which the surgical cases are charted. The duration of therapy, type of therapy and clinical course may be seen at a glance in relation to the gross and microscopic findings. There is no correlation as far as the latter are concerned with age, sex, duration or severity of symptoms before operation. The most hyperplastic glands in the group treated with thiouracil only occurred in some of the early cases when the dosage was larger than in those later in the series, but even so, extreme hyperplasia was found where the duration of treatment had been as short as 25 days or as long as 23 weeks. In general diffuse extreme hyperplasia, (*i.e.*, columnar cells with papillary infoldings, marked loss of colloid and marginal vacuolization of what remained), was observed in those glands which had had adequate thiouracil preparation and no other treatment. There were, however, exceptions even to this (Fig. 4).

These 18 glands prepared on thiouracil alone were compared with a control group of 30 prepared on iodine alone. It was somewhat surprising that the average weight of the tissue, where recorded, was found to be less in the thiouracil-treated group than in the group prepared with iodine, *i.e.*, 15 thiouracil treated glands, average 43.1 Gm.; 23 iodine treated glands average 50.8 Gm. In finer histologic detail changes in the colloid—fragmentation, change in staining, disappearance—were studied and found to be more marked in the thiouracil treated group than in those prepared with iodine. Marginal vacuolization and papillary infolding did not vary markedly in the two groups. Focal collections of lymphocytes, with or without germinal centers, appeared about equal in the two series. On first study it seemed as if the hyperplastic epithelial cells in the thiouracil group were paler and somewhat thicker, even when tall columnar. This characteristic can be seen in some of the photomicrographs (Figs. 3 and 6), but as a criterion this is not wholly reliable because of technical differences in preparation of the sections. It was almost impossible to judge accurately the vascularity in the fixed and stained preparations. It appeared, however, that the glands showing extreme hyperplasia in the thiouracil group were more vascular. Increase of fibrous tissue seemed about equal in the thiouracil group and the control.

No recognizable involutional changes were found in six of the 18 thiouracil-prepared cases. In the other 12 they were for the most part patchy and slight, but in some instances more advanced, notably in the gland which had had 52 weeks of consistent treatment (Fig. 8). An additional check on function was made by the preoperative administration of a tracer dose of radioactive iodine to two cases, (Case 1 in the toxic diffuse group, thiouracil preparation and Case 1 in the toxic nodular group, thiouracil preparation). Chemical analysis of the operative specimens revealed only a very small fraction of the radioactive iodine in the "thyroxin fraction." This is in accord with the findings of other observers.[9]

The unreliability of the histologic criteria of function is well illustrated by Figures 3 and 4, both thiouracil-treated glands with satisfactory response. The

TABLE III
SURGICAL CASES

TABLE III
SURGICAL CASES
TOXIC DIFFUSE GOITER
Thiouracil only (18 Cases)

History No. Surg. Path. No. Date of Op.	Age	Sex	Duration of Symptoms	Symptoms	Pre-Thiouracil B.M.R.	Length of Thiouracil Treatment	Preop. Days on Lugol's	Response to Thiouracil	Preop. B.M.R.	Postoperative Response and Course	Nature of Gland at Operation	Wt. of Gland Removed	Histology of Gland: Character of Acini	Histology of Gland: Lymphocytes	Fibrosis of Stroma
718766 88452 2-8-44	43	F	7 mos.	Goiter Nervous	+73	23 wks.	0	Good	+ 9	101—1st day; satisfactory	Friable; vascular	71 Gm.	Diffuse extreme hyperplasia; epithelium columnar; no involutional changes	Absent	Slight
733492 88969 3-27-44	33	F	12 mos.	Nervous. Wt. loss. Exophthalmos	+65	30 days	0	Good. Leukopenia	+ 6	102.4—1st day; satisfactory, except postop. hemorrhage	Friable; vasculat	60 Gm.	Diffuse extreme hyperplasia; epithelium high columnar; no involutional changes	Absent	None
741559 89262 4-22-44	38	F	2 yrs.	Goiter. Wt. loss—40 lb. Exophthalmos	+10	10 days	0	(Mild case) Fever	+ 3	101.4; satisfactory, except postop. hemorrhage	"no unusual findings"		Diffuse moderate hyperplasia; early involutional changes; epithelium cuboidal	Present with germinal centers	Slight
748877 90362 8-1-44	23	F	6 mos.	Goiter. Wt. loss—25 lb. Exophthalmos	+45	5 wks.	0	Fair. Leukopenia	+20	101.6—1st day; satisfactory	Firm; not vascular	36 Gm.	Patchy moderate hyperplasia with areas of involutional changes; mixed epithelium, low cuboidal predominating	Present	Marked
629879 90815 9-18-44	31	F	12 mos.	Goiter. Nervous	+69	25 days	0	Good	+36 (1 wk. preop.)	102—1st day; satisfactory	Firm; scarcely vascular	45 Gm.	Diffuse extreme hyperplasia; no involutional changes; epithelium high columnar	Absent	Slight
720569 91168 10-20-44	36	M	4 yrs.	Goiter. Palpitations. Heat intolerance	+35	52 wks.	0	Fair (alcoholic)	+ 9	101—1st day; satisfactory	Firm; not vascular	60 Gm.	Late involution; no hyperplasia; epithelium flat	None	Marked
757270 91306 11-1-44	25	F	4 mos.	Goiter. Nervous. Wt. loss—25 lb.	+61	8 wks.	0	Good	+ 4	100.6—day of op.; satisfactory	Friable; not vascular	41 Gm.	Diffuse extreme hyperplasia; no involutional changes; epithelium columnar	Present	Slight
737985 91489 11-16-44	47	F	3 mos.	Nervous. Wt. loss—30 lb. Cardiac failure	+54	35 wks.	0	Good	+10	102—1st day; satisfactory	Friable; vascular	31 Gm.	Diffuse moderate hyperplasia; areas of early involution; epithelium predominately cuboidal	Absent	Slight
760834 91539 11-21-44	44	F	12 mos.	Goiter. Wt. loss. Exophthalmos	+44	25 days	0	Good	+ 8	100.4—1st day; satisfactory	Friable; extremely vascular		Diffuse extreme hyperplasia; no involutional changes; epithelium high columnar	Present with germinal centers	None
762160 92191 1-18-45	44	M	8 mos.	Nervous. Wt. loss—23 lb. Dyspnea	+47	12 wks.	0	Good	+ 1	100.2—1st day; satisfactory	Firm; vascular	30 Gm.	Diffuse extreme hyperplasia; no involutional changes; epithelium columnar	Present with germinal centers	Slight
761944 92302 1-27-45	18	F	6 mos.	Nervous. Wt. loss—20 lb.	+38	9 wks.	0	Good	+ 3	101.2—1st day; satisfactory	Moderately vascular	30 Gm.	Diffuse moderate hyperplasia; early involutional changes; epithelium predominately cuboidal	Present	Moderate
761857 92382 2-5-45	34	F	5 yrs.	Nervous. Wt. loss—25 lb. Cardiac failure	+50	12 wks.	0	Delayed but good	+ 1	102.2—2nd day; satisfactory	Soft; not vascular	30 Gm.	Patchy slight hyperplasia; marked late involutional changes; epithelium flat and low cuboidal	Present with germinal centers	Slight
506026 92512 2-16-45	20	F	6 mos.	Goiter. Palpitations. Tremor	+57	52 wks.	0	Delayed but good	+ 4	101.2—day of op; satisfactory	Friable; vascular	21 Gm.	Diffuse moderate hyperplasia; early involutional changes; epithelium cuboidal	Present	Moderate
523510 92955 3-24-45	38	F	12 mos.	Nervous. Wt. loss—15 lb. Exophthalmos	+52	25 wks.	0	Good	+ 1	102—1st day; satisfactory	Firm; vascular	60 Gm.	Diffuse late involutional changes; no hyperplasia; epithelium flat	Present	None
758322 93201	48	F	2 yrs.	Goiter. Wt. loss—40 lb.	+49	25 wks.	0	Good. Parotitis	+ 3	105—1st day; ulcerative	Soft; not vascular	60 Gm.	Patchy moderate hyperplasia; moderate late invo-	Present	Marked

[illegible] 3-24-45				Wt. loss—13 lb. Exophthalmos						satisfactory	vascular		changes; no hyperplasia; epithelium flat		
758322 93201 4-13-45	48	F	2 yrs.	Goiter. Wt. loss—40 lb. Cardiac failure	+49	25 wks.	0	Good. Parotitis	+ 3	105—1st day; ulcerative tracheitis	Soft; not vascular	60 Gm.	Patchy moderate hyperplasia; moderate late involutional changes; epithelium flat and cuboidal	Present	Marked
778831 93926 6-11-45	48	M	2 yrs.	Nervous. Wt. loss—30 lb. Palpitations	+42	10 wks.	0	Good	− 4	102—1st day; satisfactory	Firm; not vascular	32 Gm.	Diffuse moderate hyperplasia; early involutional changes; epithelium cuboidal	Present	Slight
776072 93953 6-13-45	32	F	4 mos.	Palpitations. Cardiac failure. Auricular fib.	+71	13 wks.	0	Good	+ 2	102—1st day; satisfactory	Extremely friable; moderately vascular	40 Gm.	Diffuse extreme hyperplasia; several areas of involutional changes	Absent	None
776106 94026 6-20-45	28	F	12 mos.	Nervous. Palpitations. Dyspnea	+81	13 wks. •	0	Good	−12	100.8—day of op.; satisfactory	Soft; moderately vascular		Diffuse extreme hyperplasia; epithelium high columnar	Present with germinal centers	Moderate
								TOXIC DIFFUSE GOITER							
								Thiouracil with Iodine Preceding Thiouracil (6 Cases)							
728433 88066 1-4-44	40	F	12 mos.	Weakness. Wt. loss—25 lb. Cardiac Failure Auricular fib.	+40	6 wks.	0	Good	+ 8	101—1st day; satisfactory	Friable; vascular	87 Gm.	Diffuse extreme hyperplasia; no involutional changes; epithelium high columnar	Absent	Moderate
734956 89256 4-22-44	45	F	2 yrs.	Goiter. Nervous. Palpitations	+73	6 wks. (none 16 days before op.)	0	Poor. Agranulocytosis	+22	102.4—1st day; moderately thyrotoxic	Friable; vascular	69 Gm.	Diffuse extreme hyperplasia; no involutional changes; epithelium columnar and cuboidal	Present	Slight
748966 90439 8-9-44	44	F	4 mos.	Goiter. Nervous. Wt. loss—15 lb.	+57	6 wks.	0	Fair	+27	102—day of op.; satisfactory	Friable; vascular	62 Gm.	Diffuse extreme hyperplasia; no involutional changes; epithelium columnar and cuboidal	Present	Slight
756197 92083 1-9-45	37	F	2 yrs.	Goiter. Nervous	+58	18 wks.	0	Delayed but good	+12	100.6—1st day; satisfactory	Friable; very vascular; tissues edematous		Patchy slight hyperplasia; diffuse involutional changes; epithelium low cuboidal	Present with germinal centers	Slight
746969 92158 1-15-45	35	F	5 yrs.	Goiter. Nervous	+18	7 wks.	0	Good	+ 7	102.6—2nd day; thyrotoxic; paroxysmal fibrillation	Friable; vascular	18 Gm.	Patchy moderate hyperplasia; patchy late involutional changes; adenomatous areas; epithelium cuboidal and flat	Present with germinal centers	Slight
765404 94185 7-3-45	48	M	6 mos.	Nervous. Wt. loss—20 lb.	+72	14 wks. (then Iodine 6 wks.)	0	Delayed but fair. Neutropenia	+20	103—2nd day; stormy	Firm; not vascular	90 Gm.	Diffuse moderate hyperplasia; marked early involutional changes; epithelium cuboidal	Absent	Slight
								TOXIC DIFFUSE GOITER							
								Thiouracil with Iodine Preoperately (14 Cases)							
719438 87331 10-19-43	35	F	3 yrs.	Nervous. Tremor	+40	9 days	7	Poor. Leukopenia	+ 9	102.8—day of op.; postop. hemorrhage; stormy	Firm; not vascular	36 Gm.	Patchy moderate hyperplasia; moderate late involutional changes; epithelium cuboidal and flat	Present with germinal centers	Slight
721875 87404 10-26-43	30	F	2 yrs.	Goiter. Nervous. Wt. loss	+26	14 days	14	Poor	+16	101.6—day of op.; satisfactory	Friable; vascular	98 Gm.	Patchy moderate hyperplasia; patchy late involutional changes; epihelium cuboidal and flat	Present with germinal centers	Slight
601874 89288 4-25-44	47	M	3 mos.	Wt. loss. Auricular fib.	+44	20 days	7	Poor. Rash	+17	101.4—day of op.; satisfactory	Soft; moderately vascular	69 Gm.	Patchy moderate hyperplasia; involutional changes; epithelium cuboidal	Absent	Slight
695538 91402 11-9-44	44	F	6 mos.	Wt. loss. Weakness	+64	33 days	6	Good	+16	101.4—2nd day; satisfactory	Firm; not vascular	15 Gm.	Patchy moderate hyperplasia; involutional changes; epithelium cuboidal and flat	Present	Slight
758541 91572 11-24-44	50	F	12 mos.	Goiter. Wt. loss—50 lb. Cardiac failure	+58	32 days	15	Poor	+24	101.4—2nd day; fair; arrhythmia	Friable; moderately vascular		Patchy moderate hyperplasia; marked involutional changes; epithelium predominately low cuboidal	Absent	Moderate
723283 91869 12-20-44	30	M	6 mos.	Goiter. Wt. loss—40 lb. Nervous	+55	49 wks.	0	Good	− 4	102.4—1st day; satisfactory	Friable; vascular	58 Gm.	Diffuse extreme hyperplasia; no involutional changes; epithelium columnar	Present with germinal centers	Slight
762504 92123 1-12-45	24	F	2 yrs.	Nervous. Palpitations	+49	26 days	16	Poor. Agranulocytosis	+26	101.2—1st day; satisfactory	Firm; not vascular		Diffuse late involutional changes; no hyperplasia; epithelium flat	Absent	Slight

													dominately low cuboidal		
723283 91869 12–20–44	30	M	6 mos.	Goiter. Wt. loss—40 lb. Nervous	+55	49 wks.	0	Good	− 4	102.4—1st day; satisfactory	Friable; vascular	58 Gm.	Diffuse extreme hyperplasia; no involutional changes; epithelium columnar	Present with germinal centers	Slight
762504 92123 1–12–45	24	F	2 yrs.	Nervous. Palpitations	+49	26 days	16	Poor. Agranulocytosis	+26	101.2—1st day; satisfactory	Firm; not vascular		Diffuse late involutional changes; no hyperplasia; epithelium flat	Absent	Slight
759999 92138 1–13–45	39	F	5 yrs.	Goiter. Nervous	+47	10 wks.	9	Poor	+18	102.6—1st day; Thyrotoxic; Tachycardia, ? flutter	Firm; moderate bleeding	38 Gm.	Diffuse late involutional changes; patchy slight hyperplasia; epithelium flat	Absent	Moderate
765753 92298 1–27–45	38	F	6 mos.	Nervous. Cardiac failure	+49	22 days	11	Fair. Thyroiditis	+ 6	101.4—1st day; satisfactory	Firm; no excessive bleeding	40 Gm.	Diffuse moderate hyperplasia; marked early involutional changes; epithelium cuboidal	Present	Slight
631003 92557 2–20–45	48	F	12 mos.	Nervous. Wt. loss	+31	15 days	16	Poor	+33	101.8—1st day; satisfactory	Soft; not vascular	20 Gm.	Patchy slight hyperplasia; diffuse late involutional changes; epithelium predominately flat	Present with germinal centers	Slight
770748 93121 4–27–45	22	F	4 mos.	Goiter. Nervous. Palpitations	+53	10 wks.	10	Good	+ 9	101.8—1st day; satisfactory	Firm; not vascular	28 Gm.	Patchy slight hyperplasia; diffuse involutional changes; epithelium predominately flat	Present with germinal centers	Slight
785611 93564 5–12–45	30	F	6 mos.	Nervous. Wt. loss Palpitations	+50	16 wks.	6	Good	+ 1	101—1st day; satisfactory	Firm; not vascular	18.5 Gm.	Patchy slight hyperplasia; diffuse involutional changes; epithelium cuboidal; Hurthle cell adenoma	Present with germinal centers	Moderate
799919 95508 10–29–45	39	F	2 yrs.	Wt. loss—30 lb. Cardiac failure. Auricular fib.	+50	6 wks.	12	Good	+ 4	103—1st day; Thyrotoxic	Friable; not vascular	60 Gm.	Diffuse involutional changes; no hyperplasia; epithelium low cuboidal and flat	Present with germinal centers	None
790390 95811 11–26–45	41	F	7 yrs.	Nervous. Palpitations Exophthalmos	+35	10 wks.	15	Good	+ 6	101—day of op.; satisfactory	Firm; not vascular	65 Gm.	Diffuse moderate hyperplasia; marked early involutional changes; epithelium cuboidal	Present	Moderate
								TOXIC DIFFUSE GOITER—RECURRENT							
								Variable Preparation (4 Cases)							
701675 88965 3–24–44	23	F	2 yrs.	Nervous. Tremor. Wt. loss	+27	16 days	16	Fair	+ 9	100.8—1st day; satisfactory	Not vascular (scarring)	6 Gm.	Patchy slight hyperplasia; early involutional changes; epithelium columnar and cuboidal	Absent	Scarring
659317 91490 11–16–44	41	F	7 yrs.	Nervous. Palpitations. Wt. loss	+65	7 wks.	0	Good	+ 4	101.8—day of op.; satisfactory	Friable; vascular	39 Gm.	Patchy hyperplasia; patchy early involutional changes; adenomatous areas; epithelium columnar and cuboidal	Absent	Slight
768511 92895 3–19–45	56	F	2 yrs.	Nervous. Wt. loss—30 lb. Cardiac failure	+62	11 wks.	11	Delayed; good	+ 5	101.2—1st day; satisfactory	Friable; vascular	16 Gm.	Patchy slight hyperplasia; diffuse involutional changes; epithelium cuboidal	Present	Scarring
777107 93194 4–13–45	42	M	1 yr.	Weakness. Marked wt. loss—40 lb Cardiac failure	+67	11 days	10	Good	+ 9	103—day of op.; Thyrotoxic (insufficient removal)	Firm; vascular	30 Gm.	Patchy extreme hyperplasia; early involutional changes; epithelium columnar and cuboidal	Present	Slight
								TOXIC NODULAR GOITER							
								Variable Preparation (5 Cases—1 Recurrent)							
742623 90428 8–8–44	57	F	3 yrs.	Goiter. Nervous. Wt. loss. Sensitive to Iodine	+57	4 mos.	0	Good	+10	101.8—2nd day; satisfactory	Firm; not vascular	132 Gm.			
491350 90985 10–4–44	46	F	8 mos.	Fibrillation. Previous thyroidectomy for nontoxic nodular goiter	+46	9 days	10	Good; transient Leukopenia	+13	101—2nd day; satisfactory	Firm; not vascular				
752781 91307 11–1–44	33	F	11 yrs.	Nervous. Palpitation. Previous thyroidectomy for toxic nodular goiter	+44	10 wks.	8	Good	+14	102—2nd day; satisfactory	Friable; vascular	122 Gm.			
765068 91923 12–26–44	65	M	2 yrs.	Palpitation. Cardiac failure	+43	3 mos.	14	Good	+ 2	102.2—1st day; satisfactory	Soft; nodular; not vascular	70 Gm.			
745815 92783 3–10–45	51	F	6 mos.	Goiter. Nervous. Tremor	+51	10 mos.	14 (prior to thiouracil)	Good	+13	101.4—2nd day; satisfactory	Not vascular	45 Gm.			

UNIV. OF MICH.

one at 23 weeks shows what might be called a "classic" thiouracil response—extreme hyperplasia. The one at 28 weeks is a striking contrast. The explanation is not at hand.

CONCLUSIONS

1. Thiouracil in this series has controlled the symptoms and signs of thyrotoxicosis in all cases and restored the basal metabolic rate to normal except when prematurely discontinued.

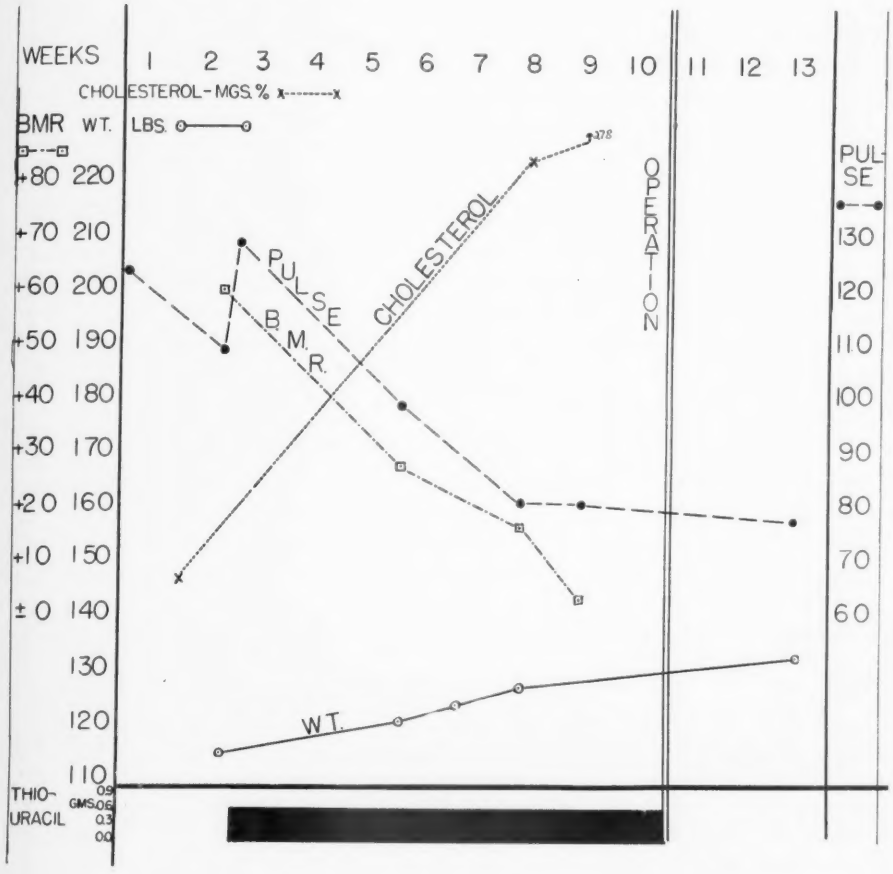


CHART I

CHART 1.—Case 7: Graph of satisfactory thiouracil response—Preoperative.

2. The incidence of "permanent" remissions obtained in primary thyrotoxicosis by the use of thiouracil is so small that we do not advocate it as the sole therapeutic agent.

3. Prolonged treatment with thiouracil in primary thyrotoxicosis should probably be reserved for the following categories of cases:

a. Those in which surgery has been refused, has been ineffective or is inadvisable.
b. Those in which malignant exophthalmos is feared.
c. Those which are in the adolescent age-group.
d. Those in which roentgenotherapy has been administered without benefit and where operation is not feasible.

4. As a preparation for operation the use of iodine alone is advocated for the average case of toxic goiter because of the present incidence of toxic reactions with thiouracil and the length of time required for preparation with this drug. (Should a related drug without toxic effects be successfully developed these conclusions might well be revised). Thiouracil can be used to advantage as preparation for operation in:

a. The poor risk cases such as thyrocardiacs or those with extreme thyrotoxicosis.
b. Patients who do not tolerate iodine or who require prolonged preoperative treatment.

5. Thiouracil therapy is promising in a selected group of cases with recurrence of symptoms after operation.

6. The permanent remissions in thiouracil treatment of recurrent toxic goiter are disappointingly few but the drug does offer a means of control of hyperactivity over long periods.

7. There is no constant correlation between the pathologic findings and the preoperative course, *i.e.*, duration, severity of symptoms and therapy.

REFERENCES

[1] Aranow, H., Jr., and Engle, E. T.: The Effect of the Administration of Thiouracil to Monkeys. (In press.)

[2] Astwood, E. B.: Treatment of Hyperthyroidism with Thiourea and Thiouracil. J. A. M. A., **122**, 78–81, May 8, 1943.

[3] Astwood, E. B.: Thiouracil Treatment in Hyperthyroidism. J. Clinic. Endocrinol, **4**, 229–248, June, 1944.

[4] Engle, E. T., and Aranow, H., Jr.: Hyperplasia of the Thyroid Gland of Rhesus Monkeys after Thiouracil Treatment. (In press.)

[5] Lahey, F. H., Bartels, E. C., Warren, S., and Meissner, W. A.: Thiouracil: Its Use in the Preoperative Treatment of Severe Hyperthyroidism. Surg., Gynec. & Obst., **81**, 425–439, October, 1945.

[6] Moore, F. D., Sweeney, D. N., Cope, O., and Rawson, R. W.: The Use of Thiouracil in the Preparation of Patients with Hyperthyroidism for Thyroidectomy. ANNALS OF SURGERY, **120**, 152–169, August, 1944.

[7] Moore, F. D.: Toxic Manifestations of Thiouracil Therapy. J. A. M. A., **130**, 315–319, February 9, 1946.

[8] Plummer, H. S.: Results of Administering Iodine to Patients having Exophthalmic Goiter. J. A. M. A., **80**, 1955, June 30, 1923.

[9] Rawson, R. W., Evans, R. D., Means, J. H., Peacock, W. C., Lerman, J., and Cortell, R. E.: The Action of Thiouracil upon the Thyroid Gland in Graves Disease. J. Clinic. Endocrinol, **4**, 1–11, January, 1944.

[10] Rawson, R. W., Moore, F. D., Peacock, W., Means, J. H., Cope, O., and Riddell, C. B.: Effect of Iodine on the Thyroid Gland in Graves Disease when given in Conjunction with Thiouracil: A Two-action Theory of Iodine. J. Clin. Investigation, **24**, 869, November, 1945.

[11] Riker, W., and Wescoe, E. C.: The Pharmacology and Therapeutic Application of Anti-thyroid Compounds. Am. J. M. Sc., **210**, 665–680, November, 1945.

[12] Van Winkle, W., Jr., Hardy, S. M., Hazel, G. R., Hines, D. C., Newcomber, H. S., Sharp, E. A., and Sisk, W. N.: The Clinical Toxicity of Thiouracil. J. A. M. A., **130**, 343–347, February 9, 1946.

[13] Werner, S. C., and Elliott, R. H. E., Jr.: Thiouracil in the Treatment of Postoperative Recurrent Toxic Goiter. Bull. New York Acad. Med., **20**, 417, July, 1944.

[14] Williams, R. H.: Thiouracil Treatment of Thyrotoxicosis: I. The Results of Prolonged Treatment. J. Clinic. Endocrinol., **6**, 1–22, January, 1946.

EARLY POSTOPERATIVE AMBULATION

KIM CANAVARRO, M.D.

NEW YORK, N. Y.

FROM THE SURGICAL SERVICE OF THE PRESBYTERIAN HOSPITAL, NEW YORK N. Y.

EARLY POSTOPERATIVE AMBULATION has been practiced on the surgical service since August, 1944. This brief presentation is a review of 500 such cases compared with 500 similar cases which were left in bed the usual 10 to 14 days. The findings are comparable with the results from similar studies carried on in other clinics.

The postoperative care of the group allowed to walk early is as follows: Once the patient has fully recovered from anesthesia, he is put up in a high head-gatch and encouraged to move about in bed as much as possible. The next morning an abdominal binder is applied and the patient is helped out of bed. He stands with help and is encouraged to take a few steps. He is again helped out of bed in the afternoon and walks a little more. The following morning he is assisted to the bathroom and thereafter is allowed up and about as desired. These patients are not allowed to sit in wheel chairs for several days but are made to walk.

The distribution of cases is as follows: 92 gallbladder and common duct cases, 150 appendicectomies, 106 herniae, 31 partial gastrectomies, and 121 general abdominal cases. About 77 per cent of these cases were closed with silk, 11 per cent with gut, and 12 per cent with cotton or other suture material. A similar group of cases not ambulated was used for comparison.

In the ambulated group there was a total of 43 postoperative complications, as compared with 93 for the nonambulated group, or 50 per cent fewer complications. Bronchopneumonia has been reduced from 6 per cent to 3.6 per cent; atelectasis from 1.2 per cent to 0.4 per cent; severe postoperative distention from 20 per cent to 0.2 per cent; phlebothrombosis from 2.4 per cent to 1 per cent; catherizations from 3.8 per cent to 3.6 per cent. In all cases excepting those which developed phlebothrombosis the complications occurring in the ambulated group were milder and resolved more rapidly than those which occurred in the group left in bed.

We have found that the incidence of phlebothrombosis has been reduced in the ambulated group, but not eliminated. There have been two cases of phlebothrombosis which should be mentioned.

One was a case of acute appendicitis who was walking on his first postoperative day and who was allowed home on his sixth. That night he returned to the Medical Service with the typical symptoms and findings of a pulmonary infarct. Following bilateral vein ligation and a stormy course he recovered.

The second was a case of cholecystitis and cholelithiasis. There were no preoperative complications. Following operation she was allowed up on the

first day and was walking on the third day. On the evening of the sixth day she noted the sudden onset of chest pain and pain in her left leg. Deep shock and death rapidly followed.

Study of this group of 500 cases of early ambulation has brought to light the following important points:

1. There is a definite reduction of all postoperative complications.
2. Less medication and rectal treatments are necessary.
3. Less nursing care is needed.
4. There is a far more rapid return to normal of the bodily functions in the group that was allowed up early.
5. The improvement in the morale of these patients is tremendous and the majority of them have been much in favor of this form of postoperative care.
6. There has been no delay in wound-healing or serious wound-healing complications.
7. There has been no increase in the incidence of postoperative hernia.
8. There is a saving in time and money to the patient and a more rapid turnover of patients per bed per month.
9. Early postoperative walking is not to be advised as a blanket formula for all patients.

Complications which should be mentioned as contraindication are: Prolonged preoperative bed rest; cardiac insufficiency; recent coronary occlusion; shock; severe anemia; hemorrhage or fear of hemorrhage; the presence or suspected presence of thrombi or emboli; cholangitis; pancreatitis; insecure anastomosis; copious tamponade; and difficult hernial repairs in which the tissues for repair are of poor quality. Simple drainage is not a contradindication nor is the presence of a Miller-Abbott tube.

Finally, if a program of early ambulation is to be undertaken, the importance of carrying it out in detail cannot be emphasized too strongly. It is most important to see that these patients are up and walking, not sitting in wheel chairs for days. The optimum time to ambulate these patients is in the first 24 to 36 hours, before complications have occurred. Later than the third day, few if any benefits are obtained and, in fact, it would be better to keep them in bed 10 to 14 days, as before, than to allow them up after the optimum time has passed.

THE EFFECT OF EVISCERATION UPON TRAUMATIC ABDOMINAL WOUNDS

SAMUEL B. CHILDS, JR., M.D.*
DENVER, COLO.

THE EXTRAPARIETAL PROTRUSION of an intraperitoneal organ through a traumatic wound of the abdominal wall is always an event of the first magnitude. Few abdominal injuries or catastrophes appear as urgent as the casualty whose wound permits loops of intestine to protrude outside the abdominal cavity. When the herniated viscera are visibly lacerated, transected, and traumatized, the occasion is even more pressing. Disruption of celiotomy wounds in civilian practice may present the same picture, and, in the operating room, the evisceration which may occur in a straining patient is always a matter of concern.

An opportunity to evaluate the effects of evisceration upon the mortality rate and the degree of shock in wounded individuals is made possible because of a relatively large series of World War II battle casualties.[1]

In a series of 3,154 traumatic abdominal and thoraco-abdominal cases operated upon in the Rome-Arno, North Apennines, Po Valley, Southern France, Rhineland and Central European campaigns, there were 312 cases of evisceration, approximately 10 per cent of the series. Evisceration, for the scope of this paper, is defined as the protrusion of an abdominal viscus, through a missile tract, to the outside of the abdominal cavity, the missile tract interrupting the continuity of all layers of the abdominal wall.

In this series each of the various intraperitoneal organs was eviscerated, and the frequency of the event, with reference to the presenting viscus, is shown in Table I.

The frequency of evisceration of an organ varied in regard to its mobility, volume, and in reference to the site and size of the tract. The small bowel alone, the omentum alone, the colon alone, and the small bowel and colon in combination, comprised 87 per cent of all eviscerations.

Mortality.—Case fatalities included were those cases which died within the echelon of the Field Hospital. Fatalities subsequent to evacuation were not included. A mortality rate, for this specific group, of 40.3 per cent was appreciably higher than the rate of 24 per cent for the total series of 3,154 cases.

A high mortality occurred when the colon was eviscerated. Such a situation was found, alone or in conjunction with other viscera, 73 times, with 42 deaths, a mortality of 57.5 per cent.

Thirty-two deaths, in 86 cases, a mortality rate of 37.2 per cent, occurred in the group in which the omentum alone was eviscerated. It should be stated,

* Formerly General Surgeon, Second Auxiliary Surgical Group.

however, that in this category, while only the omentum was eviscerated, any of the intraperitoneal viscera may have been traumatized by the wounding agent. Twenty-four of these deaths took place within the first two postoperative days, and were attributed to the shock syndrome. This term is applied to those casualties which arrived in critical condition, did not improve appreciably

TABLE I

FREQUENCY OF EVISCERATION OF VARIOUS INTRAPERITONEAL ORGANS

Viscus	No.	% Total	Deaths	Mortality Rate
1. Small bowel	123	39.4	43	34.9
2. Omentum alone	86	27.6	32	37.2
3. Colon	38	12.2	21	55.2
4. Small bowel and colon	24	7.7	14	58.3
5. Stomach	9	2.9	3	33.3
6. Liver	7	2.2	3	42.8
7. Stomach, colon, small bowel	5	1.6	2	40.0
8. Spleen	3	.96	0	00.0
9. Colon and liver	3	.96	3	100.0
10. Stomach and colon	2	.62	2	100.0
11. Liver and small bowel	1	.32	0	00.0
12. Spleen and stomach	1	.32	0	00.0
13. Spleen and colon	1	.32	0	00.0
14. No record	9	2.9	3	33.3
Total	312	100.00	126	40.3

TABLE II

CAUSE OF DEATH IN 94 FATALITIES OCCURRING IN 226 CASES OF EVISCERATION, EXCLUSIVE OF OMENTUM

Primary Cause of Death	Total	Per Cent	Day of Operation— 1, 2 Postop.	3rd P.O.	4th P.O.	5th P.O.	6th P.O.	7th P.O.	8th P.O.	9th P.O.	Over	No. Rec.
Shock syndrome	59	62.7	59									
Peritonitis	10	10.6		2		1	1	1	2	1	2	
Anuria	5	5.3			3	1			1			
Pulmonary embolus	4	4.2			1	1	1		1			
Pneumonitis	4	4.2		1		2		1				
Thrombosis inf. mesenteric vein	1	1.06	1									
Brain injury	1	1.06	1									
Intestinal obstruction	1	1.06					1					
Jaundice, edema	1	1.06							1			
No record	8	8.5		2	1	2					2	1
Total	94	99.74	61	5	5	7	3	2	5	1	4	1

following surgery, and died within the period limited by the second postoperative day. Two patients died on the ninth postoperative day from peritonitis. Both had combined perforations of stomach and colon. Of the remaining six deaths, four were ascribed to causes other than peritonitis. The cause of death was not recorded in two cases. The number of fatalities, two, 6.2 per cent of the 32 deaths, did not exceed the mortality rate of peritonitis in the over-all series of 3,154 cases. In the latter group the mortality rate of peritonitis was 12.04 per cent.[2]

The data indicated that the evisceration of omentum alone, was significant in reference to the severity of the intraperitoneal abdominal wound, and was

not significant, as an added contaminating factor, contributing to peritonitis. A subsequent allusion will be made to the effect of evisceration upon the state of shock.

Cases Exclusive of Omental Evisceration.—Exclusive of patients in which omentum alone presented, there remained 226 cases in which an abdominal organ protruded. Ninety-four deaths, a mortality rate of 41.5 per cent, occurred in this group. The primary cause of death is listed in Table II.

The ten deaths from peritonitis, 10.6 per cent of the total deaths within this group, was also no higher than the mortality figure for peritonitis for the over-all group (12.04 per cent).

The fatal incidence of pulmonary embolism was four, 4.2 per cent of all deaths in the group of 226 fatalities. Thrombosis of the inferior mesenteric vein occurred once.

The Multiplicity Factor.[3]—The numerical incidence of injury to abdominal organs, with reference to those wounded singly, or to those wounded in combination, as two, three, four, five or six, and alluded to as the multiplicity factor, is recorded in Table III. The omentum is not included as an organ in Table III.

TABLE III

RELATION OF MORTALITY TO NUMBER OF ORGANS INJURED

No. of Injured Organs	Total Cases	Lived	Died	Mortality Rate, %	No Record
Without organs injured	7	4	1	20.0	2
1 organ	97	71	24	25.2	2
2 organs	106	63	38	37.7	5
3 organs	74	28	43	60.5	3
4 organs	16	4	11	73.3	1
5 organs	8	2	5	71.4	1
6 organs	4	0	4	100.	0
Total	312	172	126		14

TABLE IV

TIME-LAG IN HOURS

226 CASES (EXCLUSIVE OF 86 OMENTAL EVISCERATIONS)

	0–6	6–12	12–18	18–24	Over 24	No Record
Total	77	94	16	6	10	23
Living	48	52	11	4	6	NR
Dead	29	42	5	2	4	NR
% mortality	37.6	44.6	31.3	33.3	40.0	

In Table III, a progressive upward trend of the mortality rate occurred, when the rate was plotted against the number of abdominal organs injured. This curve supports the contention that an index of the severity of a battle casualty was proportional to the number of abdominal organs injured.

Time-lag.—The elapsed time between wounding and surgery is referred to as "time-lag." The effect of time-lag upon mortality rate in this group of cases is reflected in Table IV.

MORTALITY IN RELATION TO TIME-LAG IN 203 CASES OF EVISCERATION OF ONE OR MORE ABDOMINAL ORGANS (OMENTUM EXCLUDED)

1944 - 1945

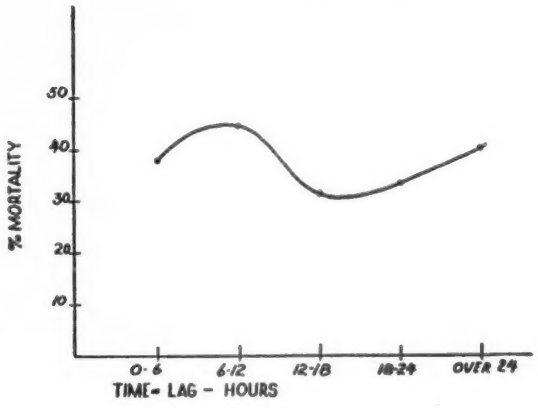


CHART I

MORTALITY IN RELATION TO TIME-LAG IN 37 CASES IN WHICH SMALL BOWEL ALONE WAS INJURED AND EVISCERATED

1944 - 1945

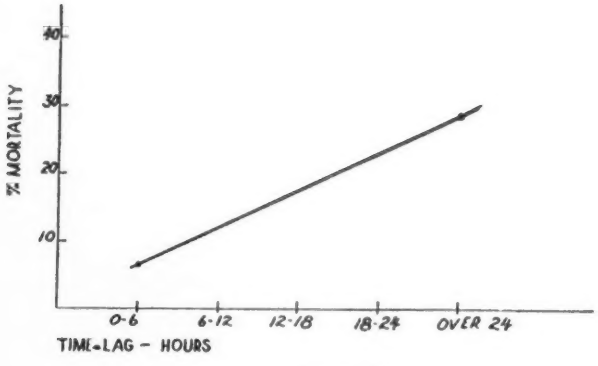


CHART II

The variable nature of this curve suggests that a large combination of factors affected it. Possibly not all of the wounded would have died within a ten-day period, if they had not been operated upon, a proposition which accounts for the survival of some in the long time-lag period, and certainly surgery had no effect in altering the lethal nature of the wound, in many of the severely wounded, although they had a short interval of time between wounding and surgery.

Evisceration of the Small Bowel.—A number of cases, involving the small bowel, presented an opportunity to consider the effects of evisceration, without the compounding effect of complex factors, because in 41 instances of the total of 123 patients in which the small bowel was eviscerated, it was the sole organ involved, and there were no complicating intra-abdominal injuries. In each of these 41 cases, the small bowel itself was wounded. Thirty-three patients lived, eight died, a mortality rate of 24.2 per cent.

Of the eight deaths, four died, within the first two postoperative days, of the shock syndrome. The rôle of peritoneal contamination, by small bowel content, may here have been manifested, because, save for the evisceration itself, none of the other complicating injuries was present. Two cases died of peritonitis on the 8th and 22nd days, respectively, one died on the 5th postoperative day, cause not stated, and the last died on the 5th postoperative day, of pneumonia.

The mortality rate of 24.2 per cent was higher than the rate in the same category, *i.e.,* small bowel alone wounded, in the 3,154 cases. In the latter series, there were 353 cases, with a mortality rate of 13.9 per cent.[4]

The average time-lag in these cases was short, 5.66 hours, indicative of the fact that these patients did not remain long in the shock ward before operation, for it was the widely held conviction that in this type of case delay in instituting surgery was futile, and the preoperative time of the administration of shock therapy was reduced to a minimum. The effect of time-lag upon mortality is shown in Chart 2. In Chart 2 only two points were plotted as otherwise numerically insignificant numbers of cases resulted.

Evisceration Without Injury to any Abdominal Organ: Five Cases.—The small bowel was eviscerated in four instances, the colon and the small bowel in one, without perforation of the lumen. The average time-lag per case was 20 hours. One fatality occurred, on the 4th postoperative day, of a massive pulmonary embolus.

Whether evisceration occurred at the time of, or subsequent to, wounding, was not indicated. However, in no instance, whatever the actual duration of the evisceration, did such a case exhibit the signs of clinical shock, either on arrival at the Field Hospital, or during the subsequent postoperative course.

The Wounding Agent and the Site of Evisceration.—In 171 patients the wounding agent was a shell fragment, in 97 a small arms bullet, in 31 a mortar, bomb, grenade, or mine fragment, and in 13 instances the agent was not recorded.

Evisceration, on occasion, occurred at the wound of entry, if the missile

was large enough. More frequently it was found at the wound of exit. In some cases, a wide-open tract existed between entry and exit wounds.

A chart of the site of evisceration of abdominal organs, without reference to omentum, reveals the upper abdomen involved 75 times, the lower abdomen 68 times, the left flank 28 times, the right flank 13 times, the left chest ten times, the right chest three times, abdominal site not specified 23 times, right back twice, left sacral region once, left buttock once, no record once.

SUMMARY AND CONCLUSION

1. Three hundred and twelve cases of evisceration were recorded; 226 of these were of an abdominal organ, 86 were of omentum alone.

2. The group mortality was 40.3 per cent.

3. Evisceration of abdominal organs occurred in five instances without other abdominal injury. No clinical shock was present in these cases.

4. The wounding agent in slightly over half the cases was a shell fragment.

5. Mortality appears to bear a definite relationship to the number of intra-abdominal organs injured.

REFERENCES

[1] Report to the Surgeon General: Forward Surgery of the Severely Wounded: A History of the Activities of the Second Auxiliary Surgical Group. August 27, 1945.

[2] Giddings, W. P., and Wolff, L. H.: The Mortality of Abdominal Wounds in Forward Hospitals. (In press)

[3] Wolff, L. H., Giddings, W. P., and Childs, S. B.: The Multiplicity Factor in the Evaluation of Abdominal Wounds. (In press)

[4] Giddings, W. P., and McDaniel, J. R.: War Injuries of the Small Intestine; *ibid:* Ref.,[1], page 238.

ORTHOPEDIC SURGERY IN THE EUROPEAN THEATER OF OPERATIONS

A BRIEF RÉSUMÉ

COLONEL MATHER CLEVELAND, M.C.
Army of the United States (inactive)
SENIOR CONSULTANT IN ORTHOPEDIC SURGERY, E.T.O.
NEW YORK CITY, N. Y.

THE PROFESSIONAL SERVICE Division of the Surgeon's office of the European Theater was established in August or September of 1942 under Major General Paul A. Hawley as Chief Surgeon and Colonel, later General, Elliott Cutler as Chief Surgical Consultant and Colonel William Middleton as Chief Medical Consultant for the Theater. Senior consultants for the Theater in all the various medical and surgical specialties were soon added. The first Senior Consultant in Orthopedic Surgery was Colonel Rex Diveley, who served as such from September of 1942 until the middle of May, 1944, when he was relieved of this assignment to devote his full-time to the Rehabilitation Division. The writer arrived in the Theater on D-Day minus 20—or about three weeks before the invasion of the Normandy beachhead—to assume the duties of Senior Consultant in Orthopedic Surgery. A tour of duty of one year at the Station Hospital at Fort Jackson had afforded an adequate background of the injuries incident to training at a large infantry post. Nine months as Orthopedic Consultant for the Fourth Service Command, with its 131 Station and 11 General Hospitals offered further opportunity to become familiar with the bone and joint problems found among the soldiers in training and returned from overseas. The earlier battle casualties with compound fractures and amputations arriving from North Africa, Italy and the Pacific were seen. At that time the vast majority of these compound fractures had been treated by the Orr-Trueta method, which left much to be desired. Returning amputees usually had not been subjected to skin traction and exposed bone ends were all too commonly encountered.

It was apparent to all surgeons of the various Theaters that there was room for improvement in the care of battle casualties with wounds involving bones and joints.

The newly arrived Senior Consultant in Orthopedic Surgery was handicapped by a lack of knowledge of the hospital and personnel situation in the Theater. Time was pressing, since the invasion was about to burst momentarily. In a period of approximately three weeks, in company with Lt. Col. William J. Stewart, who had served as assistant to Colonel Diveley between 40 and 50 hospitals were visited and the neophyte was indoctrinated to the extent that time and other circumstances allowed. Our headquarters were then in Cheltenham, later briefly in London, and even more briefly at Vallognes on the Normandy beachhead, and, finally, in Paris. The duties of a consultant who serves as eyes and ears for the Chief Surgeon and as teacher and adviser to the younger surgeons who are actually taking care

of the wounded, carries him on a constant round of visits to the various medical installations of all echelons from Field Hospital, and occasionally even further forward, back to the fixed hospitals. How many thousands of miles we covered by plane, jeep, command, or in rare instances staff car, will never be accurately known.

PRE D-DAY ACTIVITIES OF THE ORTHOPEDIC SURGEONS IN THE THEATER

The orthopedic or traumatic surgeons were a fortunate group in the Army, in that they were always busy and, therefore, on the whole, contented. The increasing Army in the United Kingdom that was training so strenuously for the invasion had many injuries of varying severity. The Air Force stationed for the most part in East Anglia sustained battle casualties from the time they became operational, and there were many compound fractures to treat.

During this period of Army training, the Medical Corps had its training program. Classes were held constantly for instruction of the officers and enlisted men. Plaster of paris technic was taught continually. There was unanimity of opinion regarding most of the plaster of paris circular splints intended for the transportation of the wounded. The Tobruk splint was the single exception. This utilization of a full-ring Thomas splint, with adhesive traction and plaster of paris reënforcement, was enthusiastically recommended by our British colleagues for transportation of compound fractures of the femur, and prior to the invasion its application was taught and advocated. Surgeons returning to the Theater from the North African campaign reported that this splint was far from satisfactory, stating that a plaster of paris spica was superior in every respect. As time passed we became more firmly convinced that the plaster of paris spica splint from the knee of the sound leg and from the toes of the fractured leg, reënforced by a posterior strut, afforded the safest and most comfortable means of immobilization of the fractured femur while in transit.

The Chief Surgeon, aided by his consultant staff, prepared a Manual of Therapy for the E.T.O. This was issued in May of 1944. This small volume contains a good deal of sound basic medicine and surgery and certain technics of treatment are described. The surgical authors were handicapped by the fact that prior experience in the case of battle casualties was limited, and in some instances nonexistent. This manual of therapy was supplemented from time to time by circular letters from the office of the Chief Surgeon as experience was gained. When V-E Day arrived, we had established a satisfactory technic for the care of battle casualties with bone and joint injuries, and all that remained was to find and place the surgeons equipped or trained to carry it out. This brings us to the next problem.

Personnel: The earliest hospitals to arrive in the Theater were affiliated units, well-staffed General, Station and Evacuation Hospitals, bursting with medical and surgical skills. Each of these early hospitals had from two to four or five officers trained in bone and joint surgery. As time went on and

the Army grew, many other hospitals were added, until, finally, there was a total of 260 hospitals in the Theater. Of these, 143 were 1,000-bed General Hospitals. The orthopedic requirements for these hospitals by Table of Organization was approximately a total of 446 medical officer specialists (3153) with a rating of "B" or "C," which was supposed to indicate full civilian training and some experience in civilian practice. To produce this number of specialists would have required a black tail coat, a silk hat and a wand. There were, in June, 1944, approximately 820 diplomats of the American Board of Orthopedic Surgery. Three hundred and one of these entered the armed services and some 63 were in the E.T.O. Six of these were immobilized as consultants or commanding officers, *etc.*, or had been returned to the Zone of Interior, so that only 57 were available for the actual care of the wounded. To supplement these "elder statesmen," there were some 95 officers who had had partial civilian training in orthopedic surgery and 85 general surgeons who had had training in traumatic surgery. The remaining officers who filled the additional 175 positions, with a specialist rating in orthopedic surgery, had received their entire training in the Army. It was a matter of grim necessity to plunder the original affiliated units, rich in trained personnel, to supply those hospitals arriving later with undertrained officers or often none capable of assuming the duty of Chief of Orthopedic Section. Since our affiliated units formed less than ten per cent of the total hospitals, the inroads on these units were heavy and constant. There was, of course, an obvious end to this sort of business of dilution of the talent. When V-E Day arrived, the sanity of the Senior Consultant in Orthopedic Surgery was just preserved, as there were some six or eight newly arrived hospitals calling for an orthopedic specialist, with none in sight. With the cessation of hostilities these frantic cries could finally be answered —"so what"? The amazing fact remains that so much creditable surgery was done with so little, relatively well-trained personnel available.

An interesting and significant wound study was made prior to D-Day in East Anglia, where Air Force casualties were received. Three parallel groups of wounds were treated as follows: (1) Adequate débridement and immediate primary closure. (2) Adequate débridement, immediate primary closure and sulfonamides. (3) Adequate débridement, immediate primary closure and penicillin. There was no essential difference in the healing in these three groups. The low incidence of infection was almost identical in each group. The one factor each group had in common was the surgical treatment and the study pointed unquestionably to the fact that surgical treatment was of paramount importance. It was of course obvious that no parallel regarding immediate primary closure of wounds existed between the Air Force personnel, wounded at high altitudes in clean surroundings, with ample opportunity to bathe, and the infantrymen, who, unwashed, in dirty clothes, were to be wounded on the heavily manured soil of France and the low countries. To close immediately wounds under these latter conditions would have been utter folly.

The Medical Corps set up to service the invasion was carefully planned. Surgical teams were assigned to the LST's and other transports that would return the wounded. Field Hospital platoons were set up on the far shore within a few days. The first Evacuation Hospitals were set up within a week after the beachhead was established.

The fixed hospitals in the United Kingdom were emptied of all except urgent cases. Surrounding the ports of embarkation there were some 15 of these fixed hospitals, which were designated as Transit Hospitals, and served for some six weeks or longer as Evacuation Hospitals for the wounded which were transportable from the far shore. These evacuable wounded had mainly extremity wounds, about half of them with compound fractures

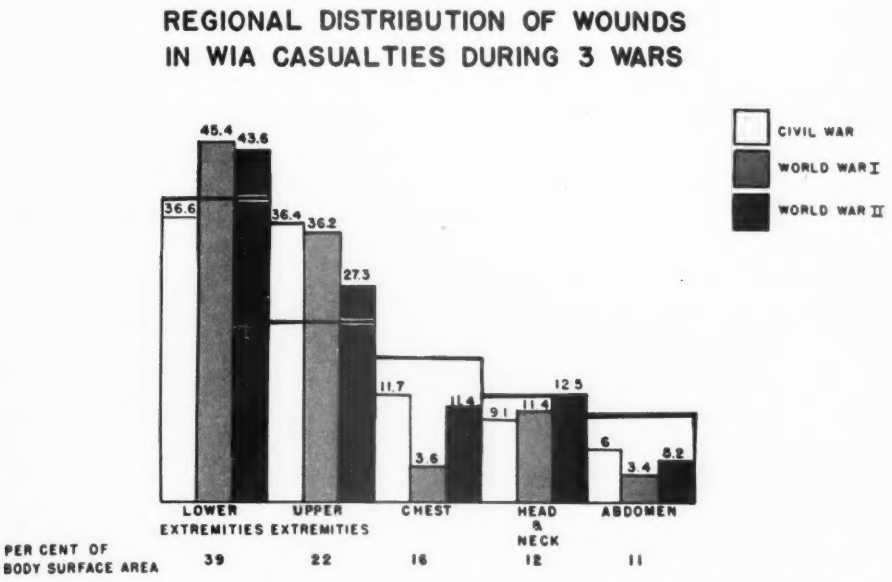


CHART I.—A table furnished by the Office of the Surgeon-General, Professional Service Division.

This comparison of the wounded in our three major wars is of great interest. The great preponderance of extremity wounds in each war is shown, 73 per cent in the Civil War, 81.6 per cent in World War I, and 70.9 per cent in World War II. Since approximately half of the extremity wounds involve bones or joints, it will be seen that between 35 per cent and 40 per cent of all battle casualties require the service of a bone and joint surgeon. Surgical personnel of all Army hospitals during hostilities should be set-up with this in mind.

The wounded and killed in action are doubtless hit in the various areas of the body in direct proportion to the per cent of total body-surface area which any part represents. These percentages of body-surface areas are indicated on the figures below the chart. It will be noted that there is a tremendous surplus of survivors in the extremity wounds and an equally marked deficit of survivors in the chest and abdominal wounds, as would be expected. The abdominal and chest wounds are apt to be immediately fatal due to massive hemorrhage.

It is interesting to note that in World War I the surviving chest and abdominal wounds were far below both the Civil War and World War II. This doubtless means that first aid and surgery had failed to keep pace with the enormously increased destructive force of the high explosive shells and high velocity small arms fire. The balance was restored in this war, despite even greater havoc and destruction wrought by the missiles used.

(Chart 1). Primary surgical treatment was administered in these Transit Hospitals, and 12 to 36 hours later the wounded were evacuated to other fixed hospitals for more definitive treatment.

The first of the fixed hospitals to accompany the invading force was opened on the far shore on August 1, 1944. The fixed hospitals which remained in the United Kingdom had, on the whole, excellent facilities and splendid equipment, and above all a stable set-up. It was to these hospitals that the bone and joint casualties, requiring a long-holding period, were evacuated.

The first fixed hospitals which moved to the continent in Normandy were under tentage. Many of these hospitals moved to a second or third site as the Army advanced. Most of them were under permanent shelter during the winter. Their facilities were for the most part not as desirable as those which they left behind in the United Kingdom, but they managed to improvise in an amazingly efficient manner. From the standpoint of the orthopedic or bone and joint surgeon, an assignment in the United Kingdom offered greater opportunity for long-time contact with bone and joint casualties than did service in the continental hospitals which served mainly on a transit basis, evacuating the compound fractures and amputees to the United Kingdom at the earliest possible moment. Only if evacuation had been or seemed likely to be unavoidably delayed beyond the optimum period for the use of skeletal traction (*i.e.,* within 21 days after wounding), were these continental hospitals permitted to treat these long bone fractures.

Air evacuation from the continent to the United Kingdom was started within the first week of the invasion and a series of Air Transit Hospitals were set up near Swindon to receive these casualties. This air evacuation, which is ideal, continued and grew in importance until finally the great bulk of the patients were transported within the Theater by this means. During December and January, the period of heavy fogs, air evacuation bogged down almost completely due to the weather. This weather "road block" is unavoidable and must always be considered.

CARE OF THE WOUNDED WITH BONE AND JOINT CASUALTIES

1. *First Aid:* So much has been written about the care of the wounded in hospitals and so little acknowledgment has been given to the devoted, skilful care which our wounded received from the corpsmen and officers at the battalion level. Many of our records state that the wounded were dressed and on the way back within 20 minutes to an hour after wounding. The great bulk of this was done by medical enlisted men. A large number of these medical soldiers and officers gave their lives in attempting to secure the high standard of care which was set for our wounded.

Splints: Compound fractures of the femur and tibia and fibula were immediately placed in the Army leg splint (a half-ring Thomas splint) with a boot strap to secure traction. This boot strap is dangerous and if applied for more than two or three hours may cause pressure necrosis over the dorsum

of the foot. Adhesive traction should be substituted if prolonged use of this splint is necessary.

For compound fractures of the foot and ankle, the well-padded wire ladder splint was used. Upper extremity compound fractures were most comfortably and effectively treated for transportation by slings or swathes. The Murray-Jones splint is dangerous to circulation and its use was pretty universally condemned.

2. *Resuscitation:* At the battalion level, plasma was available and whole blood was administered at the clearing station. It was quickly learned that whole blood alone could serve as adequate replacement where there had been massive hemorrhage. Blood was employed extensively in the treatment of these wounded at all medical installations from the clearing station to and including the General Hospitals.

3. *Army Hospitals:* The bone and joint casualties for the most part are considered transportable, so they were sent to the Evacuation Hospitals while the nontransportable abdominal and chest wounds were treated at the Field Hospitals. Primary surgical treatment was instituted in these Evacuation Hospitals.

Wound Excision or Débridement: This is easier to describe than to achieve. All possible skin should be preserved and only that obviously necrotic should be excised. The wound should be opened with adequate longitudinal incisions and exposure of underlying tissue with adequate retraction secured. A peep-hole débridement invited subsequent infection. To aid exposure and avoid any tension, the fascia should be divided longitudinally and transversely if necessary. All dead or damaged muscle or fascia must be excised, removing all dirt and available foreign bodies. All bone should be preserved. Even completely loose fragments will heal and amalgamate with the general callus if skin coverage is secured by delayed primary closure and infection does not ensue. The wanton removal of all loose bone in many instances means a complete gap or loss of bone substance which can only be substituted for by subsequent bone graft. Many of these compound fractures with numerous completely detached fragments of bone heal completely. Occasionally one or two fragments may sequestrate before healing ensues. Even if considerable sequestration takes place, the situation is preferable to an immediate complete excision of all loose bone, resulting in nonunion with loss of substance and the endless bone grafting that is inevitable.

Dressing of Wound: These compound fractures should be dressed with fine-mesh plain gauze laid over or into the wound. "Packing" of these wounds with vaselined gauze prevents drainage of blood and exudate which is inevitable and invites infection. These wounds which are adequately treated surgically, properly dressed and incased in circular plaster of paris splints and arrive with dressings undisturbed at the Communication Zone Hospitals, are ideal for delayed primary closure. There is a saying that many a patient has been bandaged to death. It is a firm conviction among those of us who observed these wounds that frequent dressing means inevitable contamination of the

wound and that the contaminated or infected wounds were perhaps more frequently infected by subsequent dressings than by the original wounding agent. Those surgeons who employed a meticulous instrument technic and wore a mask had a far higher percentage of successful closures than did those who were careless in their treatment of the wounds. Eternal vigilance and careful attention to seemingly small details paid handsome dividends in wound healing.

Chemotherapy: Those wounded with compound fractures and amputations invariably received penicillin and/or sulfadiazine from the time of primary surgery. Local use of these agents was quickly abandoned except to instill penicillin into a closed joint cavity or into the pleura. It has been quite definitely proved that in most instances penicillin is preferable and that it acts best alone.

Splinting of Compound Fractures for Transportation: Circular plaster of paris splints were prescribed, of varying types for each of the long bones involved.

1. Compound fracture of tibia and fibula—a splint extending from toes to groin.

2. Compound fracture of femur—a plaster of paris spica bandage extending from the toes of the wounded leg and from the knee of the sound leg, reënforced with a posterior strut, leg-spread no more than the width of the litter.

3. Compound fracture of forearm—a circular plaster splint extending from behind the metacarpal heads to the axilla with the wrist in slight dorsiflexion and elbow at right angle.

4. Compound fracture of humerus—a plaster of paris shoulder spica or plaster of paris Velpeau splint. In no case can the arm be abducted widely because of the limited space in ambulance, plane or hospital train.

All of these circular splints must be split to the skin and slightly spread to allow for swelling in transit. Failure to observe this rule made the responsible officer subject to disciplinary action. There were reported losses of extremities due to unsplit plaster splints from other Theaters prior to D-Day, so this Theater was able to profit from the experience of others and insist on this rule.

The Army hospitals were not held responsible in any sense for reduction of these compound fractures. That was a function reserved for the Communication Zone hospitals.

FIXED HOSPITALS IN THE ZONE OF COMMUNICATIONS

Delayed Primary Closure of Wounds: Here begins the definitive surgical treatment of the casualties with wounds involving the bones and joints. Delayed primary closure of these wounds in increasing numbers, as time went on, was the outstanding improvement in the care of these casualties. The idea of delayed primary closure of wounds is not new. It was practiced with success to a limited extent during World War I, but it was pretty well forgotten

unfortunately, as most of the lessons of military surgery are apt to be. They gather dust in a number of massive volumes, called in our particular case the Surgeon-General's history. The new crop of military surgeons usually have to learn all over again the hard way. At the outset of this war, our surgeons were dominated by the closed-plaster technic of treatment of compound fractures. This invites infection of bone and soft tissue and healing ensues slowly by second intention, with massive granulations which develop into scar tissue. Most of the earlier casualties with wounds involving bones and joints were returned to the Zone of Interior with their wounds suppurating under circular plaster splints. So firmly ingrained was the idea of closed-plaster technic, that it was not a little difficult to persuade the medical officers at first to attempt closure of these compound fractures. Within a month or six weeks after the invasion started, delayed primary closure was fairly completely accepted, and with experience it became increasingly successful.

The optimum time for delayed primary closure by suture or split-thickness skin graft is three to five days after wounding, and any time up to ten days is considered early. At this period the wound edges are mobile and the skin can readily be drawn together. After ten days there is some granulation tissue and new epithelium to be excised with some undercutting of the skin edges in order to secure approximation. A careful secondary débridement or a few days of wet dressings may be required prior to the later attempted closure. This closure by suture is accomplished by widely-spaced, deeply-placed nonabsorbable sutures without tension. Hemostasis must be secured, and at times a small drain is left in the wound for 24 to 48 hours. No attempt is made to secure a cosmetic result.

If the delayed primary closure is successful, the advantages which accrue are manifold—underlying exposed bone is conserved and healing of bone and soft-tissue is accelerated. Repair of divided peripheral nerves, open reduction of fractures, bone grafts where indicated, may all be performed at an early period. Convalescence is shortened. In an effort to determine the success of this form of treatment, 5,042 compound fractures, excluding bones of the face and skull and spine with spinal cord injury, were studied at the 15th Hospital Center between D-Day and November 15, 1944, a 4.5-month period. The bones of the lower extremity were involved in 2,614 instances and those of the upper extremity in 1,895. The long bones most frequently fractured by various missiles were the tibia (757), humerus (702), and femur (684), in that order and number.

Delayed primary closure was attempted in 2,393 patients, by suture in 2,087, by skin graft in 236, and by combination of suture and skin graft in 70. Skin grafting was by split-thickness free grafts and also by pedicle grafts where loss of bone and soft-tissue was considerable.

The results obtained in these attempted closures were as follows:

1. *Complete success*—healing by primary intention occurred in 1,592 cases, or 66.53 per cent of the total.

2. *Partial failure* occurred in 640 cases, or 26.74 per cent of the total.

Those rated partial failures showed a small sinus, a stitch abscess, or partial loss of a skin graft. All but a very few of these wounds healed by a second suture or skin graft or spontaneously and were classed as healed when the patient left the hospital. This means that a total of 93 per cent of the patients upon whom closures were attempted left the hospitals with their wounds healed.

3. *Complete failure* occurred in 161 cases, or 6.73 per cent of the total. This means an entire breaking open of the wound or the development of a soft-tissue infection or osteomyelitis, which necessitates wide surgical opening.

Further follow-up on these attempted delayed primary closures of wounds performed in the European Theater after return to the Zone of Interior was furnished by the Office of The Surgeon-General. A small series of 34 compound fractures of the femur, tibia, fibula and humerus, treated in the European Theater by delayed primary closure of their wounds were reported by the Ninth Service Command as follows: The delayed primary closure was successful in 73.5 per cent of the cases and the incidence of osteomyelitis was 14 per cent. A similar-sized series of compound fractures upon whom no attempt at closure had been made was reported also by the Ninth Service Command, showing an incidence of osteomyelitis in 54 per cent of these wounds.

There can be no question that delayed primary closure of these compound fractures can be successfully accomplished in almost three out of four cases attempted and that, if it is successful, the incidence of osteomyelitis is sharply reduced. This is in addition to the other beneficial results enumerated above.

TREATMENT OF LONG BONE FRACTURES

Long bone fractures were treated by skeletal traction, usually with Kirschner wire. An Army half-ring splint, with Pearson attachment, was utilized for balanced suspension. These long bone fractures were for the most part evacuated to fixed hospitals in the United Kingdom Base where the evacuation policy allowed a holding-period up to 120 days, whereas that period on the continent was 60 days maximum. It was our plan to hold these compound fractures in traction, following closure of the wounds until sufficient "freezing" or union had taken place, so that they would not displace when placed in circular plaster of paris splints for evacuation to the Zone of Interior. This holding-period varied from five to 12 weeks and even longer if necessary, depending upon the bone involved. Our principal error was in fractures of the shaft of the femur and trochanteric fractures which were not held in some instances sufficiently long prior to evacuation to the Zone of Interior, and displaced within the circular plaster splints with resulting malunion. Fortunately, this was quickly called to our attention and every effort was made to remedy this particular situation. Malunion in these badly damaged long bones all too often cannot be immediately avoided.

HEALING OF COMPOUND FRACTURES

A report from 19 named General Hospitals on compound fractures due to wounds treated in the European Theater was received from the Surgeon-General at the request of the Chief Surgeon of the Theater. This report

was formulated during the month of December, 1944, so that the oldest cases reported were six months or less after being wounded. From the standpoint of union of the fractures, these 3,190 patients showed the following status of healing of their fractures:

2,189, or 68.6 per cent, were satisfactorily united.
417, or 13.3 per cent, were united in malposition.
2,606, or 81.9 per cent, —total united.
584, or 18 per cent, were ununited.

It was too early to consider all of the ununited fractures as nonunions. There was, however, a sizable group that due to the loss of bone by the original wounding agent, or to the overzealous removal of loose bone fragments by the inexperienced surgeon resulted in nonunion, requiring bone grafts to bridge the gap.

AMPUTATIONS

The only amputation allowed in the Theater was the circular type which is considered an emergency measure. This amputation was done at the lowest possible level where a viable stump could be expected. It is really an inverted cone. The skin is divided in a circular manner and allowed to retract, the muscles are then divided at the level of the retracted skin, and they, in turn, retract still further and the bone or bones are divided transversely at the level of the retracted muscle. Traction is applied to the skin immediately and continued until the patient arrives at the Amputation Center in the Zone of Interior. If the amputation is performed for clostridial or other infection, skin traction is not applied for 24 to 48 hours, at which time it should be possible to determine whether the stump is infected or clean.

It was urgently insisted that continuous skin traction be maintained. This is best accomplished by weight and pulley over the foot of the bed while the patient is in the fixed hospital and by means of a plaster of paris pylon with a wire ladder splint incorporated while the patient is in transit. Stockinette fixed to the skin by Ace, or other adherent substance, and elastic cord or tubing were almost universally utilized. The amputee was usually advised that his amputation was necessary after consultation and that the procedure done in the Theater was an emergency measure which would require revision at the Amputation Center.

The amputations performed in the 3rd United States Army from August 1, 1944, to February 1, 1945, a six-months' period, were analyzed by Colonel Charles Odom, Surgical Consultant of that Army. There were 1,365 amputations performed upon 1,290 patients. Since 1,012 of these amputees were United States Army personnel among 64,389 battle casualties for that period of time, the incidence of amputation in this army was a little over 1.5 per cent of the wounded. Seventy-six per cent of the amputations occurred in the lower extremity, which is probably an indication of the efficacy of the land mines encountered. The causes of amputation were as follows: Traumatic amputation 66 per cent. Blood vessel injury 20.2 per cent. Clostridial infec-

tion 13.8 per cent. In the Army area the mortality among these 1,290 amputees was about nine per cent.

There are in World War II about 14,000 surviving major amputees among an estimated 8,000,000, or more, soldiers mobilized. In contrast to this, during the American Civil War, the Union and Confederate armies mobilized perhaps a total of three million men. There were 27,000 amputees in the Union Army and almost 25,000 among the Confederates, and the mortality in patients requiring this procedure at that time was approximately 25 per cent.

With the decrease in amputation as a means of treating the badly damaged extremity in battle casualties, there has been a corresponding increase in the compound fractures salvaged for treatment as outlined above.

THE WOUNDED HAND

The serious nature of these wounds was appreciated early and efforts were made to expedite their evacuation to Hand Centers which were set up on the continent and in the United Kingdom. These damaged hands were often immobilized too long and too extensively, with resulting swelling and fibrosis. There was at times undue delay in transferring them to the Hand Centers where plastic and orthopedic surgeons were available to secure healing of the wound and early return of function. In an effort to avoid this prolonged rigid immobilization, the wounded hand was considered chiefly from the standpoint of its soft-parts. A pressure dressing, with the hand and fingers in functional position, was recommended, with elevation of the part and early closure of wounds by suture or skin graft—split-thickness or pedicle as required.

In March of 1945 we decided to try immediate loose primary closure of these wounded hands in all possible cases in the Army hospitals (Evacuation Hospitals for the most part). A careful and complete scrubbing of the wounded hand and a meticulous débridement were insisted upon prior to the immediate primary closure. The hand that had been sutured had to be held nonevacuable for five days. These regulations were put in effect in mid-April, 1945, and within a few weeks hostilities ceased. As an indication of what might be expected from this form of treatment, two surgeons in different Evacuation Hospitals reported immediate primary suture on a total of 80 hand wounds, with only five wound infections occurring. This was a vast improvement over delayed primary suture, and with early healing, rehabilitation of the wounded part could be commenced at an earlier period from the time of wounding.

Every effort was made to salvage one or two useful fingers in the severely damaged hands. No tendon replacement or bone grafts were undertaken in the Theater. Patients requiring this type of surgery were returned to the Zone of Interior. The prompt amputation of one or even two irretrievably damaged fingers with shattered bones and joints and severed flexor tendons will often afford the early salvage of an excellent three- or four-finger hand. With only one finger lost a soldier can be fairly promptly returned to full

duty. Early in the campaign a good deal of useless effort was expended in attempts to save one badly damaged finger—to the detriment of the hand.

Wounds Involving Joints: These wounds are always troublesome and potentially dangerous. Their proper treatment is based on sound basic surgical principles. Lt. Colonels Thompson and Cassebaum and Captain Stewart presented two important reports on the treatment of these joint wounds. The joint wound should be carefully explored through adequate incisions, all devitalized or damaged soft tissue and bone excised, all foreign bodies found in the joint cavity or overlying soft tissues should be removed and the joint gently lavaged. The capsule should be closed immediately by suture or fascial graft if necessary. The overlying soft-tissue wound is left open to be closed later by delayed primary closure. Twenty thousand units of penicillin are instilled into the closed joint cavity. Immobilization of the joint is secured by adequate and prescribed plaster of paris circular splint with a window for inspection of the joint should need arise. The patient with such a wound must be held nonevacuable for seven to ten days, during which time he receives parenteral penicillin, 20,000 units every three hours. If necessary, an additional 20,000 units of penicillin is injected into the joint cavity at 24-hour intervals. If healing proceeds uneventfully, the superficial wound is closed three to five days after primary surgery was done. By this treatment a high percentage of joint wounds were salvaged with useful motion.

In the irretrievably damaged joint or where infection is developing, an early resection of the joint will promote healing of the wound. In the joints of the lower extremity and wrist, fusion or arthrodesis is the goal to be sought, with the joint in the position to secure optimum function in the remaining mobile joints. In the elbow and shoulder joints after resection and healing of the wounds, early mobilization will give a surprisingly good range of motion with useful though by no means complete stability.

COMBINED NEUROSURGICAL AND FRACTURE PROBLEMS

Approximately 75 per cent of the compound fractures complicated by nerve lesions occur in the upper extremity with the compound fracture of the humerus and injury to the radial nerve comprising the vast majority of these. The compound fracture of the femur with division of the sciatic nerve is fortunately not very frequently encountered, forming perhaps ten per cent of the total of these combined injuries. There is apparently no means of ascertaining in the first few weeks after wounding whether a nerve has been divided or merely badly contused. A high percentage of the nerves explored required only a neurolysis. The Senior Consultant in Neurosurgery, Colonel Glen Spurling, and the Senior Consultant in Orthopedic Surgery were in accord that the divided or potentially divided major peripheral nerve should be given precedence over the compound fracture.

The plan of treatment of these combined nerve and fracture problems was as follows: They were transferred immediately to a Neurosurgical Center. The wound was closed by delayed primary suture or skin graft. The fracture was meanwhile placed in balanced suspension. No effort was made to secure

anatomic length because this might defeat the attempt to get the nerve ends together. Three weeks after wound-healing had ensued, the nerve was explored and sutured if found divided. If it were necessary in order to get the nerve ends together, the bone was shortened up to 2.5 cm. This shortening was not frequently required. In the humerus it was of no moment, and in the few cases of the femur which required shortening, little or no disability due to the procedure was anticipated. These openly reduced fractures were treated by internal fixation. Needless to say, penicillin was quite extensively employed in these combined surgical procedures.

OBSERVATIONS ON THE COMPARISON OF MEDICAL CARE OF THE WOUNDED IN WORLD WAR I AND WORLD WAR II

Having served as a medical officer in both wars, it may be permissible to make a few comparisons. The 25 years which elapsed between the wars has seen progress in the training of the young surgeons and this was reflected in the fact that more and better trained surgeons were available to do better surgery. There never were enough to completely fill all the existing vacancies, but the situation was vastly improved over World War I. In the European Theater the general level of care of bone and joint casualties was vastly improved. Superior care was unquestionably rendered by many of the affiliated hospitals in World War I, but in other less favored units it left much to be desired.

There was a more complete and general understanding of resuscitation in World War II. No blood or plasma was available or used in most of the Army hospitals in World War I. The great stocks of plasma and whole blood which were made available and were used so extensively saved many of the wounded who would otherwise have succumbed.

The evacuation of the wounded in World War II was more rapidly accomplished.

The overseas hospitals were very much better equipped for their work in this war.

The low incidence of infection was probably due to better surgery in the forward areas. In this matter of lower infection, the rôle of sulfonamides and penicillin is not absolutely clear. These new drugs probably exerted a beneficial effect, but controlled experimental data is not available.

The European Theater was singularly fortunate in having a Chief Surgeon whose sole aim was to improve the standard of care of the sick and wounded American soldier. Nothing deterred him from this aim. The professional service division had a group of consultants who worked harmoniously as a team under inspiring leadership of the Chief Surgeon and the Chief Consultants in Surgery and Medicine.

REFERENCE

[1] Cleveland, Lt. Col. Mather; Grove, Maj. John A., M.C., A.U.S., Delayed Primary Closure of Wounds with Compound Fractures. J. Bone and Joint Surg., Vol. xxvii, No. 3, pp. 452-456, July, 1945.

LAMINECTOMY FOR POTT'S PARAPLEGIA

EDWIN M. DEERY, M.D.

NEW YORK, N. Y.

FROM THE NEW YORK ORTHOPEDIC HOSPITAL, NEW YORK CITY, N. Y.

IT IS GENERALLY AGREED that about 90 per cent of all Pott's paraplegia patients will recover, given appropriate orthopedic care. The tendency in the past has been to consider the remaining 10 per cent hopeless.

Laminectomy has more often been withheld, than applied, in such cases, but the operation is finding a limited use. Seddon[1] reviewed a series of 25 laminectomies for Pott's paraplegia. With ten postoperative deaths, nine unimproved and six recoveries, he considered the results "appalling." Steindler,[2] however, in a group of 12 patients subjected to laminectomy, found seven relieved of their paraplegia. He believes the operation does have a limited use in the treatment of refractive cases of paraplegia.

The ill repute of laminectomy in Pott's paraplegia has come from the high mortality figures of the past, as many patients died from surgical shock. The operation at present, even in these often debilitated patients should carry no particular risk from shock. Laminectomy for spinal cord tumor or nucleus pulposus herniations, at present involves practically no risk from shock. Patients with Pott's paraplegia are by no means good risks, but death from shock after laminectomy should rarely occur.

Mechanically, laminectomy in Pott's disease has been strongly objected to because of the already diseased and weakened ventral elements of the spinal column. This objection cannot be held valid if fusion, either spontaneous or operative, has been achieved before the laminectomy is carried out, nor, considering the unfavorable nature of the group, can laminectomy be objected to in unfused patients, if spine fusion is performed at the time of the laminectomy.

A group of 23 consecutive cases, in which laminectomy was performed for Pott's paraplegia at the New York Orthopedic Hospital have been reviewed. These patients were considered by the staff to be among the 10 per cent generally considered hopeless. The paraplegia, which was usually severe, had failed to respond to the usual orthopedic measures. Fifteen of these patients showed a spinal manometric block with an elevated protein. Six had a high protein but no manometric block. One had a normal manometric test with a normal protein. Lumbar puncture was not carried out in one case.

Fifteen of the patients had had surgical fusion, and one had developed spontaneous fusion, before a laminectomy was decided upon. In the remaining seven unfused cases, spine fusion was carried out at the time of the laminectomy.

Disregarding, for the moment, such modifying factors as age, and the type of intraspinal lesion found, the results were as follows: Eight patients had a good result. They were walking well when last heard from. Three

patients were improved. They could walk with various degrees of difficulty. Ten were unimproved by operation. The follow-up period varied from a few months in a few, to as much as 11 years in others. There were two deaths, but neither of these was from surgical shock. A child died four weeks after laminectomy from tuberculous meningitis. It is possible that this condition was beginning, though unrecognized, at the time of operation. An adult negro died 33 days after laminectomy. Necropsy showed very wide spread, long-standing tuberculosis of many viscera. It is difficult to classify this as a postoperative death, in the usual meaning of the term.

In deciding whether these results be good, bad or indifferent, it seems fair to repeat that this group represents the 10 per cent of Pott's paraplegia, generally considered to be hopeless. It is not unreasonable to believe that any result better than hopeless is a step in the right direction.

Of the 15 adults, three obtained a good result, whereas, of eight children operated upon, five had good results. The figures from this group suggest that laminectomy for Pott's paraplegia is more hopeful in children.

The intraspinal lesions found at operation were the three well-recognized conditions described in the literature. Eight patients had a thick, localized mass of granulations surrounding the dura. Eight had, as far as could be determined, compression of the cord ventrally by the diseased vertebral bodies. Seven patients proved to have an intraspinal, extradural cold abscess. The good results showed no relation to the type of intraspinal pathology—three, having granulations, three, compression of the cord ventrally by bone, and two, having cold abscesses.

Of the eight good results, six were obtained in patients with an early onset type of paraplegia (paralysis developing in the first two years of the disease). Two good results were obtained in the late onset type of paraplegia. However, of the total of 23 cases, 14 were of the early onset-type of paraplegia. No relationship between the type of paraplegia and the result from laminectomy can be shown from these figures.

The location for the laminectomy was, in every instance, determined by the sensory level present. Actually, in all cases, the sensory level, the intraspinal pathology and the apex of the kyphos all corresponded very closely.

There is little to be said about the technical aspects of the laminectomy except to stress the fact that it was made for decompression only. The cold abscesses were aspirated, as far as possible, but the other two types of lesions were strictly undisturbed. The laminectomy in every case was made rather longer and narrower than would ordinarily be made for other neurosurgical problems. This was in respect to the already existing fusion in some, or to permit satisfactory fusion when carried out at the time of the laminectomy. The dura was never opened because of the presence of tuberculosis.

A group of 23 patients with refractive Pott's paraplegia received a decompressive laminectomy. The results are briefly stated for record purposes, rather than as an argument for, or against, the operation. The neurologic surgeon sees little of the problems of tuberculosis, but given a patient with

refractive Pott's paraplegia, particularly if a spinal manometric block be present, it seems difficult to withhold a decompressive laminectomy.

REFERENCES

1 Seddon, H. J.: Pott's Paraplegia: Prognosis and Treatment. Brit. Jour. Surg., **22**, 769–799, April, 1935.

2 Steindler, A.: Paraplegia in Pott's Disease. Journal-Lancet, **54**, 281–286, May, 1934.

INDICATIONS AND RESULTS OF SURGERY OF THE AUTONOMIC NERVOUS SYSTEM IN NAVAL PERSONNEL*

LT. COMDR. E. N. GOODMAN, M.C., U.S.N.R.,
LT. W. J. MESSINGER, M.C., U.S.N.R.,
AND
CAPT. J. C. WHITE, M.C., U.S.N.R.

THE INDICATIONS FOR SURGERY of the sympathetic nervous system in Naval personnel, arranged in order of their relative importance, have been:

A. Causalgia of the classical "Weir Mitchell" type.
B. Pain after amputation.
C. Peripheral vascular disease.
   1. Raynaud's syndrome.
   2. Thrombo-angiitis obliterans.
   3. Vasospasm with arteriosclerosis.
   4. Thrombophlebitic complications with vasospasm.
   5. Vasospasm following injury to major arteries.
D. Hyperhidrosis.
E. Hypertension.
F. Angina pectoris.

The methods of study have been recorded individually. Operative procedures used by this group have been those formulated by Capt. J. C. White and Reginald Smithwick.[18] Completeness of preganglionic sympathectomy has been measured by elevated cutaneous resistance changes, (measured by Richter's[15] dermometer), by paralysis of the sweat glands (determined by Victor Minor's[12] starch-iodine test), and by objective signs of an asymptomatic hot, dry, extremity.

A. CAUSALGIA

Methods of Study.—We have included in this group only those cases which conform to the picture of major causalgia described by Mitchell, Morehouse, and Keen,[13] and we quote excerpts of their classical description:

"Recently we have seen numbers of men who had burning pain without glossy skin, and in some we have seen this latter condition commencing. The burning comes first, the skin change afterward; but in no case of great depravity in the nutrient condition of the skin have we failed to meet with it, and that in its forms of almost unendurable anguish. The terms here used may seem strong to those who have not encountered these cases; but no one who has seen them will think that, as regards some of them, it would be possible to overstate their most wretched condition. The seat of burning pain is very various; but it never attacks the trunk, rarely the arm or thigh, and not often

* This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the U. S. Navy. The opinions and views set forth in this article are those of the writers and are not to be considered as reflecting the policies of the Navy Department.

TABLE I

RELIEF OF CAUSALGIA BY PREGANGLIONIC SYMPATHECTOMY

Case	Wound	Paralysis	Distribution of Pain	Time of Onset After Wounding	Hyperpathia	Trophic Changes	Temperature of Extremity	Sweating
1. Charles C.R. Pfc. USMC	Small shell fragments left upper arm	Median N. (partial)	Entire hand	Few hours	+++	+++	Cool	+++
2. Fred S. Pvt. USMC	Shell fragments upper arm and forearm	Median N. (partial). Ulnar N (complete)	Entire hand	Five hours	+++	++	Cool	+++
3. John H. Major USMC	Upper humerus fractured by shell fragment. Aneurysm	Median N. (complete). Ulnar N. (partial)	Entire hand	Immediate	++	+	Cold	+
4. Norman C. Pfc. USMC	Machine gun bullet passed between 2 upper forearm bones	Median N. (partial)	Entire hand	Few hours	+	+++	Cool	++
5. Charles M. Pfc. USMC	Rifle bullet through upper arm. Artery severed	Median N. (partial)	Median distribution		++	+	Cold	++
6. Nathan V. Pvt. USMC	Rifle bullet through forearm. Fractured ulna	Median N. (partial)	Median distribution		+	+++ (median area)	Cold	++
7. Robert B. Col. USMC	Bullet wound brachial plexus. Fractured clavicle, severed artery	Median and ulnar N's (partial). Medial antebrachial cutaneous N's (complete)	Entire hand	1 week	+++	++	Cool	0
8. Alfred D. Pfc. USMC	Mortar wound medfan side of arm, axilla to mid forearm	Median N. (partial)	Median area of hand	Day after wound	+++	+	Cool	+
9. Howard W. Pfc. USMC	Bullet wound below elbow	Median N. (partial)	Median area of hand	Immediate	++	+	Cold	+++
10. Harold O'S. Pfc. USMC	Shell fragment wound of internal condyle of elbow	Ulnar N. (partial)	Ulnar area of hand		++	+	Cold	+++
11. Donald McC. Lt.(jg) USNR	Through and through shrapnel wd. lower ⅓ L. thigh	Common peroneal N. injury	Foot volar area and toes	Immediate	++++	++	Cool	+++
12. John B. GM 2/c USNR	Razor laceration right hand	Median N. (partial)	Median distribution	After nerve suture	+++	++	Cool	+++
13. William M. Cpl. USMC	Shrapnel wound right popliteal space	Post-tibial (partial)	Entire foot	Few hours	+++	+	Cool foot	++

TABLE I

RELIEF OF CAUSALGIA BY PREGANGLIONIC SYMPATHECTOMY

	Distribution of Pain	Time of Onset After Wounding	Hyperpathia	Trophic Changes	Temperature of Extremity	Sweating	Relation to Cold	Relation to Emo
	Entire hand	Few hours	+++	+++	Cool	+++	+++	++
	Entire hand	Five hours	+++	++	Cool	+++	+++	++
lete)	Entire hand	Immediate	++	+	Cold	+	++	++
ial)	Entire hand	Few hours	+	+++	Cool	++	++	0
	Median distribution		++	+	Cold	++	++	++
	Median distribution		+	+++ (median area)	Cold	++	+	++
nar chial	Entire hand	1 week	+++	++	Cool	0	++	++
	Median area of hand	Day after wound	+++	+	Cool	+	++	++
	Median area of hand	Immediate	++	+	Cold	+++	++	++
	Ulnar area of hand		++	+	Cold	+++	++	++
	Foot volar area and toes	Immediate	++++	++	Cool	+++	+++	+++
	Median distribution	After nerve suture	+++	++	Cool	+++	++	++
	Entire foot	Few hours	+++	+	Cool foot	++	++	++

eat-g	Relation to: Cold	Emotion	Operations in Addition to Sympathectomy	Result of Sympathectomy
-+	+++	+++	Early median neurolysis overseas without any improvement	Complete relief; now plays strenuous games
-+	+++	+++	Subsequent median neurolysis and ulnar N. suture	All hyperesthesia cleared; sl. residual ache in finger tip
	++	+++	Aneurysmorraphy median N. Will require suture later	Complete relief
+	++	0	Previous neurolysis and partial suture of median N., with partial relief	Complete relief
+	++	++	None	Complete relief
+	+	++	Neurolysis median N., without relief	Complete relief
	++	+++	None	Hyperpathia of hand gone but at times sl. residual pain in elbow and wrist
	++	++	None	Complete relief at 6 weeks
+	++	++	Previous median neurolysis	Complete relief at 6 weeks
+	++	++	None	Complete relief
+	+++	++++	Débridement and neurolysis—common peroneal	Complete immediate relief
+	++	++	Suture of nerve	Complete relief
-	++	+++	Neurolysis post-tibial nerve	Partial relief after removal L-2 and L-3. 80% relief after transperitoneal removal of remaining lumbar ganglia. Complete relief after neurolysis

UNIV. OF MICH.

the forearm or leg. Its favorite site is the foot or hand. In these parts it is to be found most often where the nutritive skin changes are met with; that is to say, on the palm of the hand, or palmar face of the fingers, and on the dorsum of the foot: scarcely ever on the sole of the foot or the back of the hand. The part itself is not alone subject to an intense burning sensation, but becomes exquisitely hyperaesthetic, so that a touch or a tap of the finger increases the pain. Exposure to the air is avoided by the patient with a care which seems absurd, and most of the bad cases keep the hand constantly wet, finding relief in the moisture rather than in the coolness of the application. Two of these sufferers carried a bottle of water and a sponge, and never permitted the part to become dry for a moment. As the pain increases, the general sympathy becomes more marked. The temper changes and grows irritable, the face becomes anxious, and has a look of weariness and suffering. The sleep is restless, and the constitutional condition, reacting on the wounded limb, exasperates the hyperaesthetic state, so that the rattling of a newspaper, a breath of air, another's step across the ward, the vibrations caused by a military band, or the shock of the feet in walking, give rise to increase of pain. We feel that we may be supposed to have exaggerated somewhat in delineating these hitherto undescribed neural disorders. Surgeons who have happened to encounter a single one of the worst of them, have been so surprised at the character of the suffering as to suspect that such extreme hyperaesthesia must be due, at least in some measure, to a desire on the part of the patient to magnify his pains. If we be not mistaken, this form of neuralgia is hitherto undescribed. Perhaps no pen can do it justice without the more life-like details of cases."

In classical causalgia, the condition of the patient precludes practical quantitative methods of evaluating symptoms. In Table I, the symptoms of this group are noted. If these symptoms have been relieved by paravertebral procaine block, preganglionic sympathectomy has been performed with consistently successful results. A classical case is cited in detail:

Case Report.—Charles C., Pvt., U.S.M.C.R.—Age 21: The patient was injured on Okinawa by a booby-trap explosion. Fragments of the bomb entered the forehead, right thigh and left arm without serious injury or loss of consciousness. He was evacuated to the rear and four hours after injury he developed marked burning pain in the left forearm and hand with evidence of incomplete injury to the median nerve. On June 18, 1945, the median nerve of the left arm was explored and neurolysis performed, without alleviating causalgic symptoms. The patient continued in extreme constant distress. This consisted of diffuse burning pain in the left forearm and hand, made worse by any type of emotional disturbance, such as radio, movies, loud talking, *etc.*, and also by exposure to cold. The patient could not be kept in an open ward, but required a quiet room where he constantly either soaked his hand in warm water or wrapped it in wet towels. He was unable to use the extremity because of the extreme hyperpathia. On July 14, 1945, a paravertebral procaine block of ganglia T2 and T3 resulted in complete temporary relief from symptoms. A thoracic preganglionic sympathectomy was performed three days later, with immediate and complete relief of causalgia. Ten days after operation, the patient was playing volley ball.

Discussion on Causalgia.—There are various theories as to the etiology of causalgia. Our cases favor the theory of Doupe, Cullen and Chance,[4] who state: "The qualities of causalgic pain are due to direct cross-stimulation of sensory fibers by afferent sympathetic impulses at the point where the nerve trunk is injured." This theory provides an explanation for the severe hyper-

pathia which occurs in cold environment, as a result of excitement or cutaneous stimulation, and, as demonstrated by some of our cases, by defecation, micturition (Case 1), and swallowing cold liquids (Case 5). Experimentally, Katz and Schmidt[8] have corroborated the theory of sympathetic activation of sensory fibers by demonstrating that, under specified conditions, efferent nerve impulses can alter the excitability of adjacent sensory axones. Direct experimental proof of cross-stimulation between motor and sensory fibers at point of nerve injury has been demonstrated by Granite, Legksell, and Skoglumd.[5] These workers, with the aid of the cathode ray oscillograph have recorded the afferent discharge from a sensory root which occurs when an injured motor root is stimulated.

Our patients in this group presented evidence of overactivity of the sympathetic nervous system. Their hyperpathia was made worse by lowering of environmental temperature, by increased emotional excitement induced by noise, exciting movies, and noisy radios. One patient suffered severe hyperpathia from micturition and another from drinking cold water. If operation is to be successful in this group of patients, preganglionic sypmathectomy must be complete.

In case, for example, the removal of two distinct ganglia at the side of the 2nd lumbar vertebra only relieved the burning hyperesthesia in the proximal two thirds of the foot. Vestiges of sweat secretion and a suspiciously low electrical skin resistance induced us to try procaine block at the level of the 3rd and 4th lumbar vertebrae. This abolished all residual pain in the toes, and the effect was thought to have been made permanent by removing an anomalous lower ganglion at the side of the 3rd vertebra. However, the patient soon began to complain of pain and burning in the ball of the foot. This was completely relieved by procaine block of the posterior tibial nerve. Neurolysis revealed a slight scar about this nerve, and the patient is now symptom-free. Relief by this procedure again suggests anomalous sympathetic fibers.

B. PAIN AFTER AMPUTATION

Other than Local Tenderness of a Neuroma

Methods of Study.—The methods were essentially the same as those listed for the causalgia group, and have been directed to evaluate the rôle of the sympathetic system. Whenever relief of pain was obtained after paravertebral procaine block, the patient was subjected to preganglionic sympathectomy. The data of such patients is found in Table II.

All these patients had had peripheral amputations, mostly of the fingers or toes. It is, of course, in this region that the release of vasoconstrictor tone after sympathectomy is most pronounced. Furthermore, all the cases in this group presented evidence of increased vasomotor phenomena and the patients had cold, sweaty extremities. Their pain was aggravated by lowered environmental temperature, but not by emotional stimuli. The character of this type of pain after peripheral amputation has consisted of a deep aching with a diffuse hyperthesia at times involving a whole limb. It was not similar to the

TABLE III

PERIPHERAL VASCULAR DISEASE

RAYNAUD'S SYNDROME

Pt.	Presenting Symptoms	Duration of Symptoms	Pertinent Findings	Operation	Result of Operation
20. Donald R. M3c USNR Age 29	Pain in both fingers and finger tips, increased by cold. Blanching on exposure to cold. Superficial ulceration tips. R. 3rd and 4th fingers, L. 4th finger. Pain in feet on exposure to cold	1 yr.	Mottled blue cold fingers on exposure to cold. Ulceration. Hyperhidrosis hands and feet. Normal pulsations. Normal oscillometric readings	Bilat. Thoracic preganglion sympathectomy. Lumbar sympathectomy. Bilateral	Warm dry hands and feet, loss of sensitivity to cold. 2 months
21. Harry O'D CM3c USNR Age 36	Redness of fingers with blanching. Severe pain in fingers on exposure to cold	28 mos.	Dead white fingers after 3 min. exposure to cold water. Cyanosis hyperhidrosis. Normal pulsations. Roentgen rays neg. No cervical rib; hyperhidrosis	Bilateral preganglionic thor. sympathectomy	Excellent circulation; both hands dry and warm. 5 mos.
22. Joseph DeC. A.S. USNR Age 22	Painful R. hand, arm, aggravated by cold and excitement. Marked intermittent swelling of R. hand	4 mos.	Both hands cold, blue and hyperhidrotic. Marked pain and blanching in R. hand and forearm with ice water immersion. Normal pulsations. Oscillometric readings normal. No cervical rib; hyperhidrosis	R. thoracic preganglionic sympathectomy	Warm dry pink R. hand. Loss of cold sensitivity. 2 mos.
23. Herbert M. S1c USNR Age 19	Painful, cold, blue hands. Intermittent severe painful swelling of L. palm	3 mos.	Both hands cold, blue, hyperhidrotic. Marked blanching of hands in elevation and delayed return in dependency. L. palm puffy and tender. Abscess of nail bed L. index finger. All pulses present in all positions. Oscillometric readings normal. No cervical rib. Extreme pain in L. hand on immersion in ice water with marked blanching of L. fingers	L. thoracic preganglionic sympathectomy	Warm dry pink L. hand. Loss of all sensitivity. Less sweating of R. hand. 2 mos.

THROMBO-ANGIITIS OBLITERANS SYNDROME

24. Maurice D. RDM1c Age 24	Claudication walking 2 blocks. Necrotic ulcer, paronychia 4th left toe	3 mos.	Cool sweaty feet with cyanosis on dependency, blanching on elevation. Absence of D.P.* P.T.† bilaterally and R. popliteal. Oscillometric readings diminished in R. calf and both feet	Bilateral lumbar sympathectomy. L1, L2	Prompt healing of ulcre and paronychia. No claudication. No change in pulsations or oscillometric readings
25. Seymour B. Pfc. USMC, Age 22	Pain lower legs and feet on walking, improving with rest		Absent pedal pulses. Marked blanching on elevation and delayed cyanosis on dependency. Marked hyperhidrosis both feet	Bilateral lumbar sympathectomy. L2, L3	Feet dry and warm. Pain relieved 2 mos.
26. Seth J. S1c USNR Age 20	Pain and swelling of L. foot		Absent pedal pulses and L., P.T. Ulceration of L. toe. Both feet cold and cyanotic. Marked pallor on elevation with slow return of color on dependency	L. lumbar sympathectomy. L1, L2, L3	Foot warm and painless with prompt healing of ulceration. 3 mos.
27. Harry W. QM1c Age 33	Cyanotic L. foot swelling and tenderness	1.5 yrs.	L. foot cyanotic and cold, absent D. P. bilaterally. Absent P.T., L. Severe blanching of L. foot on elevation with slow return of color on dependency	L. lumbar sympathectomy. L1, L2, L3	Warm foot, free of pain and swelling, 4 mos.
28. Lewis W. VAP Age 52	Pain L. ankle on walking with decreased exercise tolerance in L. leg. Can walk farther after alcoholic	6 mos.	L. popliteal and D.P. absent. No calcified vessels by roentgenray. No improvement in exercise tolerance following paravertebral procaine sympathetic block	L. lumbar sympathectomy. L1, L2	Can walk ½ mile without claudication, with occasional cramps in L. calf

* D.P.—Dorsalis pedis pulse.

†P.T.—Posterior tibial pulse.

	Claudication walking 2 blocks. 3 mos.		Cool sweaty feet with cyanosis on dependency, blanching on	Bilateral lumbar sympa-	Prompt healing of ulcre
D. RDM1c Age 24	Necrotic ulcer, paronychia 4th left toe		elevation. Absence of D.P.* P.T.† bilaterally and R. popliteal. Oscillometric readings diminished in R. calf and both feet	thectomy. L1, L2	and paronychia. No claudication. No change in pulsations or oscillometric readings
25. Seymour B. Pfc. USMC, Age 22	Pain lower legs and feet on walking, improving with rest		Absent pedal pulses. Marked blanching on elevation and delayed cyanosis on dependency. Marked hyperhidrosis both feet	Bilateral lumbar sympathectomy. L2, L3	Feet dry and warm. Pain relieved 2 mos.
26. Seth J. S1c USNR Age 20	Pain and swelling of L. foot		Absent pedal pulses and L., P.T. Ulceration of L. toe. Both feet cold and cyanotic. Marked pallor on elevation with slow return of color on dependency	L. lumbar sympathectomy. L1, L2, L3	Foot warm and painless with prompt healing of ulceration. 3 mos.
27. Harry W. QM1c Age 33	Cyanotic L. foot swelling and tenderness	1.5 yrs.	L. foot cyanotic and cold, absent D. P. bilaterally. Absent P.T., L. Severe blanching of L. foot on elevation with slow return of color on dependency	L. lumbar sympathectomy. L1, L2, L3	Warm foot, free of pain and swelling, 4 mos.
* D.P.—Dorsalis pedis pulse. †P.T.—Posterior tibial pulse.					
28. Lewis W. VAP Age 52	Pain L. ankle on walking with decreased exercise tolerance in L. leg. Can walk farther after alcoholic drink	6 mos.	L. popliteal and D.P. absent. No calcified vessels by roentgenray. No improvement in exercise tolerance following paravertebral procaine sympathetic block	L. lumbar sympathectomy. L1, L2	Can walk ½ mile without claudication, with occasional cramps in L. calf foot warm. Pt. has returned to job for mos.
29. Harry F. VAP Age 43	Claudication in calf muscles. L. greater than R. Severe L. foot pain, trophic ulcer L. leg 2 yrs.	3 yrs.	Cyanosis both feet with marked blanching on elevation. Bilateral cold and hyperhidrotic feet. Absent D.P. bilateral. Absent P.T. on R. Marked decrease of oscillometric readings in calves and feet	L. lumbar sympathectomy. L1, L2, L3	Prompt healing of trophic ulcer. Warm foot. Complete relief of claudication
30. Rudy K. Lt. Cdr. USNR Age 44	Severe claudication L. calf. Coolness L. foot. Impending gangrene 1st L. toe	1 yr.	Sharp temp gradient at L. ankle. Coolness and hyperhidrosis L. foot. Impending gangrene 1st L. toe. Diminished circumference L. calf. Marked blanching on elevation. Marked rubor on dependency. Zero oscillometric readings L. foot and calf. Absence of both D.P. and L., P.T. art. No calcified vessels by roentgen-ray	L. lumbar sympathectomy. L1, L2	Warm dry foot. Area of impending gangrene cleared in 9 days. Exercise tolerance markedly increased with improvement progressive. No change in oscillometric readings but L., P.T. pulse is intermittently palpable
31. Joseph	Fourteen-month history of painful,	14 mos.	Evidence of migratory phlebitis on lower extremities. Cold	Bilateral thoracic sym-	Prompt healing of ulcera-

			Absence of both D.P. and L., P.T. art. No calcified vessels by roentgen-ray		increased with improvement progressive. No change in oscillometric readings but L., P.T. pulse is intermittently palpable
31. Joseph L. MoMM2/c Age 36	Fourteen-month history of painful, cold, discolored fingers R. hand. Painful R. leg. Calf claudication on moderate walking	14 mos.	Evidence of migratory phlebitis on lower extremities. Cold tender ulcerated R. 4th and 5th fingers with color changes. Tenderness over ulnar art. R. Marked rubor both hands with severe blanching on elevation. Decreased oscillometric readings on L. forearm. Moderate rubor of both feet. Absent D.P. and P.T. Feet cold and hyperhidrotic. Oscillometric readings decreased in calves and feet	Bilateral thoracic sympathectomy. Bilateral lumbar sympathectomy. L1, L2	Prompt healing of ulcerations and immediate relief of pain of fingers. Warm dry hands—minimal color changes. Warm dry feet with progressive loss of claudication
			ARTERIOSCLEROSIS WITH VASOSPASM		
32. Michael O'H MM1c Age 45	Cramping pain calf L. leg	2 mos.	All peripheral pulse present but D.P. reduced on L. Feet cold. Sweating marked. Roentgen-ray, mild calcification of arts. both legs	L. lumbar sympathectomy. L1, L2	Warm L. foot with increase in D.P. Marked increase in exercise tolerance without claudication 2 mos after op. free of pain. Good toe color, warm foot, returned to work
33. Harry M. VAP Age 47	Sudden sharp pain R. foot and ankle. Cold and painful R. foot	1 mo.	R foot cyanotic. Circulation of R. 1st, 2nd, 3rd toes poor with impending gangrene of 2nd toe. Absence of D.P. and P.T. R.; calcified arteries R. calf by roentgen-ray. All 4 extremities cool and sweaty	R. lumbar sympathectomy. L1, L2, L3	
			THROMBOPHLEBITIC COMPLICATIONS WITH VASOSPASM		
34. Gyger C. SC2c Age 28	Pain L. leg after thrombophlebitis	1 mo.	Vasospasm, excessive sweating, L. greater than R. Decreased P.T., L.	L. lumbar sympathectomy. L1, L2	Foot hot and dry. Sufficient relief of symptoms to request duty, 3.5 mos.
35. Ahearn B. F1c Age 32	Pain aggravated by walking. Pain interfering with sleep. L. leg thrombophlebitis	18 mos.	Excessive sweating feet. Feet cool. Swelling L. leg	L. lumbar sympathectomy. L1, L2, L3	Warm dry foot. Leg symptom free, below knee with sl. ache above knee

UNIV. OF MICH.

burning hyperpathia of major causalgia. Symptoms complained of by the patients summarized in Table II are quite different from those seen with a mechanically irritated neuroma, phantom limb, or the episode of lancinating pain or bursting pain occasionally encountered in the major amputation neuralgias. These conditions have recently been discussed by one of us,[19] and require an altogether different form of treatment.

TABLE II

RELIEF OF LOCAL PAIN AFTER AMPUTATION BY INTERRUPTION OF SYMPATHETIC FIBERS

Case	Condition	Surgical Procedures	Relief
14. Henry J. CM3c USN	Traumatic amputation of distal phalanges of 4th and 5th fingers. Very cold, cyanotic, sweaty hands	(1) Paravertebral procaine block. T1—T2 (2) Upper thoracic preganglionic sympathectomy	Temp. relief. Warm hand and arm free of former deep pain at discharge. (3 weeks)
15. John G. S3c USN	Traumatic amputation 2nd and 3rd fingers. Local hyperesthesia in 3rd finger had been relieved by excision of neuroma, but without effect on neuralgia of hand and forearm	(1) Paravertebral procaine block. T1—T2 (2) Upper thoracic preganglionic sympathectomy	Temp. relief. Complete relief of ascending neuralgic pain. Pt. still complained of hypersensitive index finger, but was able to return to limited duty
16. Philip C. Sgt. USMC	Traumatic amputation tip of 5th finger with repeated amputations to metacarpal level for local hyperesthesia and deep ache in hand and arm. Cold, cyanotic hands	(1) Procaine block of upper thoracic ganglia (2) Upper thoracic preganglionic sympathectomy	Relief for 2 hours. Nearly complete relief of deep aching pain in hand and arm at 3 months
17. Henry C. S2c USNR	Traumatic amputation 3rd toe with severe pain in stump and bottom of foot. Aggravated by cold, not by psychic stimuli	(1) Paravertebral procaine block, L2—L4 (2) Lumbar sympathectomy, L2—L3	Temporary relief Complete relief at 2 months
18. James L. A.S. RN	Traumatic metatarsal amput. with pain in stump running up to knee. Deep ache in left foot. Deep ache worse in cold weather. All 4 extremities involved in vasospasm. Left foot cold and sweaty	(1) Procaine paravert. L. block (2) Lumbar sympathectomy L-1-2-3	(1) Foot hot and dry, pt. comfortable (2) Complete relief of symptoms, return to orthopedic service for repair of stump
19. Henry C. S2c USNR Age 24	Traumatic amputation 3rd right toe with pain in stump which continued after revision of stump. Foot cold and cyanotic. Hyperesthesia over lower ½ foot	(1) Procaine symp. block, L-2-3 (2) Lumbar sympathectomy L-1-2-3	(1) Pain disappeared with complete vasodilatation (2) Complete relief of symptoms

C. PERIPHERAL VASCULAR DISEASE

Methods of Study.—These patients were first studied on the Medical Service, and when it was apparent that the problem was one of peripheral vascular symptomatology, the following methods were used for detailed investigation:

The extremities in question were observed for color and rapidity of change in color resultant from changes in position; for differences in temperature; absence of peripheral pulses; oscillometric readings; degree of sweating; and presence or absence of arterial calcification roentgenologically. Changes in temperature and color of the digits and extremities before and after procaine block of the sympathetic efferent fibers either by paravertebral injection of procaine, spinal anesthesia, or peripheral nerve block were recorded in a room of nearly constant temperature.

It should be added, parenthetically, that in thrombo-angiitis obliterans an

increase in collateral circulation and reduction of intermittent claudication will often follow preganglionic sympathectomy, even though no striking improvement can be demonstrated during the brief period of vasoconstrictor paralysis which follows procaine block. As stated by White and Smithwick,[18] sympathectomy is generally worth a routine trial in younger individuals who have not lost their femoral pulse and do not have infection or painful gangrene.

Discussion of Peripheral Vascular Group.—This group of patients with peripheral vascular disease, which falls into a number of categories, all have well-defined vasospastic phenomena, in common.

1. *The Raynaud's Syndrome:* This group of patients have vasopastic disorders with color changes, but not necessarily advanced to the stage of dead-white fingers. As Lewis first pointed out, when the disease has advanced to the stage of pallid asphyxia of the fingers during exposure to cold, this phenomenon is not caused by extreme vasoconstriction, but by local changes in the walls of the digital arteries. The few biopsies which have been secured have all shown the presence of a true endarteritis obliterans.[18] The complication of a dead-white finger and also the association of scleroderma will minimize the good results that otherwise might be obtained from preganglionic sympathectomy. It should be recognized that the Raynaud's phenomena may cover a wide range of vasomotor and sudomotor disturbances, from the cold, wet, cyanotic hands, in which there are no endarteritic changes (Plate IA), to the cold, white, dry hand resembling that seen in advanced occlusive vascular disease. In the former, preganglionic sympathectomy gives uniformly gratifying results, but naturally when endarteritic changes have occurred, the results are less satisfactory. Therefore, emphasis must be placed on early diagnosis and operation. The applicability of these facts is well demonstrated in our cases (See Table III). We are aware of the criteria of Allen and Brown,[1] recently reëmphasized by Hines and Christensen,[6] for the accurate diagnosis of Raynaud's disease in men. However, we are of the opinion that if one waits for the Raynaud's phenomena to progress to the so-called Raynaud's disease, the most opportune time for operation will have been lost.

2. *Thrombo-angiitis Obliterans:* In this group, it is our opinion that optimum results are obtained in those patients who have no sepsis or gangrene, and who have femoral pulsations. If recognized early, preganglionic sympathectomy will afford immediate satisfactory results. In this group, studied at the Massachusetts General Hospital, the incidence of amputation has been reduced from 50 per cent to 10 per cent.[18] Pain in thrombo-angiitis obliterans associated with sepsis or gangrene is best treated by preliminary peripheral nerve crush, which gives in effect a temporary sympathectomy.[17] When this procedure is followed by healing of the ulcer with general improvement of the extremity, pregangionic sympathectomy is indicated.

In our group, there have been instances of impending gangrene in which restoration of adequate circulation through preganglionic sympathectomy resulted in prompt healing (Plate IB). It is striking to observe the complete relief of painful symptoms and the rapidity of tissue restoration in these indi-

PLATE I

A

Thrombo-angiitis obliterans (Case 31).
A. Status of fingers on day before sympathectomy.

B

B. Appearance of fingers ten days after R. thoracic sympathectomy. Only slight discoloration of 4th and 5th R. finger tips is visible and gangrenous ulcers are completely healed.

viduals (Fig. 2) in contrast to the results of lengthly treatments other than sympathectomy. There have been no amputations in our small series. We are not in agreement with Montgomery,[14] who states that sympathectomy is of no use when the vessels are no longer capable of dilation, for our cases demonstrate that if only the femoral arteries are patent, preganglionic sympathectomy is good prophylaxis in protecting the new collateral vessels from vasoconstricting influences. While our cases have not had the benefit of lengthly follow-up, it is evident that they have been physically and economically rehabilitated within a few weeks and none have suffered amputations. It should be noted that all these patients have been advised to cease the use of tobacco in any form and to use alcohol in therapeutic doses. An interesting case history is quoted in detail:

Case Report.—Joseph L. Momm 2c, U.S.N.R.: Thrombo-angiitis obliterans.

In May, 1944, this 36-year-old white male complained of soreness of right knee followed by cold and painful right big toe. In turn there followed painful right instep and ankle aggravated by hikes. In July, 1944, patient complained of cramp-like sensation in right ankle followed by right palmar pain. By November, 1944, he began to shirk work due to a painful right ankle and he noted discoloration and coolness of right midleg region. A few weeks later patient was hospitalized and treated for thrombo-phlebitis of right leg. In April, 1945, the 4th and 5th fingers of right hand were noted to be cold and painful and a month later ulceration of nail bed of 5th right finger was noted. One week later, tip of 4th finger ulcerated. Patient was treated for fungus infection of finger tips and returned to U. S. for demobilization. At Separation Center he complained of claudication of legs and extremely painful discolored ulcerated 4th and 5th fingers of right hand which patient described as "stone cold." Pertinent physical findings on admission to this hospital were classical signs of thrombo-angiitis obliterans of all four extremities, with ulcerations of 4th and 5th right fingers. Right thoracic procaine paravertebral block gave immediate relief of symptoms and a warm, dry hand. Following preganglionic thoracic sympathectomy, immediate relief of symptoms was obtained and healing of the ulcerations of the 4th and 5th right fingers was complete by 4th postoperative day. At suitable intervals, right and left lumbar sympathectomies were done on this patient with good results, and he no longer had claudication in his legs.

3. *Arteriosclerosis with Vasospasm:* Preganglionic sympathectomy can only be expected to give satisfactory results in this group if there is evidence of excessive sympathetic tone. If the extremity is cold and moist and there is a fair response to a temporary block of the sympathetic outflow, preganglionic sympathectomy offers a reasonable chance of increasing the effective circulation of the extremity. Case 32 represents a satisfactory response to this operation.

4. *Thrombophlebitic Complications with Vasospasm:* These cases were instances of thrombophlebitis in which, after the acute process had subsided, there remained edema, pain, and evidence of vasospasm. They presented cold, sweaty extremities which became warm, dry and painless after sympathetic block.

5. *Vasospasm Following Wounds of Major Arteries:* Numerous reports have appeared in the past year dealing with wounds of major vessels.[2, 3, 16] In

a personal communication to one of us (J. C. W.), Brigadier Ogilvie* stated that he had seen no successful cases of popliteal ligation in the African Desert campaign, without added sympathectomy.

One of our patients (James W., age 27, Slc) suffered injury and severance of his left popliteal artery by shrapnel. Following ligation he had a cool left leg and foot, claudication of calf muscles, and hyperhydrosis of the foot. All symptoms were relieved by procaine block of L1,2,3. After lumbar sympathectomy, the foot was warm, pink, and dry, the pedal pulse increased in volume, and he complained only of slight calf ache on walking.

D. HYPERHYDROSIS

Both of our cases obtained satisfactory relief from preganglionic sympathectomy (Table IV). Hyperhydrosis is most common in young, emotional people in whom there is usually circumstantial evidence of a psychosomatic

TABLE IV

HYPERHIDROSIS

Pt.	Presenting Symptoms	Duration of Symptoms	Pertinent Findings	Operation	Result of Operation
36. Thoreau W. Pfc. Age 26	Excessive sweating feet with cold blue feet in cold weather. Had filiarisis	1 mo.	Cold hyperhidrotic feet, cyanosis feet. Pulsations intact. Chr. dermophytosis feet	Right lumbar sympathectomy	Hot dry right foot. Back on guard duty 3 mos.
37. Larson P. RM3c Age 25	Hyperhidrosis of hands with maceration palms	yrs.	Extreme hyperhidrosis. Feet to lesser degree	Bilat. thoracic preganglionic sympathectomy	Warm, dry hands. 4 mos.

disorder. The symptoms have been most incapacitating in stenographers and medical students, and those handling delicate fabrics. Although these people are not suitable for the armed forces, they can be rehabilitated for civilian occupations by preganglionic sympathectomy.

E. HYPERTENSION

Methods of Study.—The persistence and range of abnormally elevated blood pressures in our patients was observed over a sufficient period of time to rule out anxiety states, combat fatigue, metabolic disturbances and hypertension of known endocrine origin. Methods used for evaluation of renal function were the P. S. P., urea clearance, concentration tests and frequent examinations of the urine. Intravenous pyelogram studies ruled out gross structural kidney changes and retrograde pyelography and perirenal air insufflation studies were used as supplementary procedures when indicated. Range of alteration of blood pressure, as a measure of the reactivity of the sympathetic nervous system, was measured by the use of the cold pressor test of Hines,[7] the sodium amytal sedation test, and in some of our patients by the standardized "two-step test" of Masters.[10, 11] Examination of the fundi was carried out by a competent ophthalmologist and the findings graded according

* British consultant to Montgomery's Army.

to the classification of Keith, *et al.*[9] The results of radical thoracolumbar sympathectomy in 14 patients are summarized in Table V. Two interesting case histories are cited in detail:

Case 1.—Robert R., age 35, Lt., U. S. N. R. (Case 51). Hypertension.

For six months prior to admission to the hospital in 1945, the patient began to notice easy fatigability followed by headaches of three months' duration and blurring of vision and nocturia of one month duration. Ten days prior to admission he had suffered a series of convulsions, amnesia, and fell out of bed, injuring his forehead. Familial history revealed that his father was suffering from angina pectoris and occlusive vascular disease, with the loss of a lower extremity.

Physical Examination.—The fundi showed papilledema and blurred disk margins; old "cotton wool" hemorrhages were seen and some scars of old hemorrhages. The fundi were classed as Grade III. The heart was judged to be normal and roentgenograms revealed no increase in size. The E. C. G. was thought to be significant of coronary disease. Neurologic examination was normal. The urine contained 1+ albumen and concentrated to a sp. gr. of 1.021. N.P.N. was 34.5 mg. per cent. I.V.P. was normal. Events are now best noted in chronologic order.

5-19-45: Convulsions. Intraspinal pressure 390 mm. H_2O.

5-21-45: B/P.— Lying 200/130 Sitting 190/140 Standing 200/150

6-4-45: Convulsion yesterday and this A.M.

6-7-45: Right thoracic lumbar sympathectomy—kidney and adrenal palpated and found to be normal.

6-15-45: Complains of more blurring of vision. Has vertigo, faintness and headache which makes it impossible to get him up.

P.S.P. 55° N.P.N. 40 Urine sp. gr. 1.015

6-16-45: B/P. 200/120

6-22-45: Left thoracolumbar sympathectomy. Renal biopsy. B. P. 70/40 after operation.

6-24-45: B/P. 180/120 to 150/110. Fundi show great many more recent hemorrhages-exudate.

7-1-45: B/P. 150/90 to 160/100. Patient noting subjective eye improvement.

7-2-45: Up walking—no orthostatic failure.

7-8-45: B/P. — Lying 146/90 Sitting 136/90 Standing. 130/80 Intraspinal pressure 220 mm. H_2O.

7-31-45: Remarkable improvement

8-14-45: B/P. Sitting 155/110 to 145/110 Standing 145–135/100 Smoking 2 cigarettes 155/120

Feels well—swims—skips rope.

12-21-45: B/P. Sitting 160/120 Walking 3 flights of stairs 170/120 to 160/120

Disks have nearly returned to normal. Vision good, still tires easily, occasional headaches, no orthostatic hypotension.

1-7-46: B/P. 180/120 to 160/110, no difference in positions.

Told interesting story of how prior to his cerebral crisis, he had worked out an important device for the Navy in connection with radar electronics. He had entirely lost track of his work after the cerebral crisis. Since returning to his desk after operation, he was able to pick up the threads of the idea again.

2-8-44: B/P. 170/100.

8-1-44: Working hard at M.I.T. for Navy — tires easily — B/P. 160/130.

11-27-44: Readmitted — B/P. 168/118 to 196/128. Heart not enlarged—A2 greater than P2, normal rate and rhythm. N.P.N. 36, Urine Alb. 0, Casts 0, sp. gr. 1.020. Fundi normal, except for narrowed vessels with nicking.

TABLE V

HYPERTENSION

Name	Duration of Symptoms	Pertinent Findings	Operation	Result of Operation
38. Ruth D. Age 31	6 yrs.	Easy fatigibility, headaches, irritability, florid face. Grade II eyegrounds. Cardiovascular system normal. Renal function good. Heart not enlarged. ECG L. ventricular strain. BP 240/190 — — —. 130/130 Good sedation test	Bilat. thoracolumbar sympathectomy. T10—L2	Improvement in eyegrounds; less irritable and nervous. BP 140/160 — — —. 88/96
39. Francis H. VAP Age 44	1 yr.	EP 200 irritable. Eyegrounds grounds Grade II. Cardiovascular system normal. Renal function good. Heart not enlarged by roentgen-ray. Had 2 hypertensive cerebral crises 3 wks. before op.	Bilat. thoracolumbar sympathectomy. T10—L1, R. T9 —L1, L.	BP 140/160 — — —. 3½ 90/100 mos. Returned to work as shipping clerk
40. Margaret H. Age 31	4 yrs.	Severe headaches and precordial pain relieved by rest. Irritable with occ. blurring of vision. Normal C-V system. Heart not enlarged. ECG normal. Fundi Grade I. BP 175 —. Abnormal cold pressor 100 test	Bilat. thoracolumbar sympathectomy. T10—L3, R. T10—L2, L.	BP 118/132 — — —. 76/80 Emotionally stable 14 mos. General sense of well-being. Renal biopsy—chr. vascular nephritis Grade III
41. James G. VAP Age 47		Cerebrobvascular crises. BP 140/190 — — —. 98/120 Eyegrounds Grade II	Bilat. thoracolumbar sympathectomy. T9—L1, R. T9—L2, L.	125/140 — — —. 6 mos. 100/110 General sense well-being. Renal biopsy, chr. vascular nephritis Grade III
42. Anna G. Age 47	6 yrs.	Severe headaches, vertigo, easy fatigability. Eyegrounds Grade II. BP 220 —. ECG normal. Renal 130 Renal function tests good. Chest normal	Bilat. thoracolumbar sympathectomy. T10—L2	BP 180 —. 10 mos. less 100 nervous and irritable. Returned to light work.
43. Thomas B. Age 55	3 yrs.	Nervousness, headaches, irritability, tinnitus, vertigo of 3 wks. duration. Eye grounds Grade II. BP 188/206 — — —. Cardiovascular 108/116 system normal. Sclerosis and tortuosity aorta by roentgen-ray. Renal function good. ECG normal	Bilat. thoracolumbar sympathectomy. T9—L2, R. T8—L2, L.	Returned to active Naval duty—6 mos. BP 150 —. Doing light 100 duty 11 mos., no further reduction in BP.
44. Lillian I. (Mrs.) Age 34	2 yrs.	Nervousness, vertigo, headaches, blurring vision. BP 168/210 — — —. Eyegrounds, 110/140 Grade II. Normal cardiovascular system and ECG. Slight impairment renal function. 3 mos. pregnant with past history of several miscarriages	Bilat. thoracolumbar sympathectomy. T8—L2, R. T9—L2, L.	Operation done during early mos. of pregnancy. Stroke during 7th mo. of pregnancy but with excellent recovery. Normal baby. Throughout pregnancy BP 130 —, but thereafter 90 it rose to 180 —. 100
45. Helen M. (Mrs.) Age 41	10 yrs.	5 stillborn children. Eyegrounds Grade II. Nervous. BP 215/240 — — —. 112/140 Heart slightly enlarged with systolic murmur at apex. ECG shows cardiac changes, compatiable with hypertension. Renal function aver.	Bilat. thoracolumbar sympathectomy. T9—L3, R. T6—L2, L.	Striking postural hypotension. At 9 mos. back to work. BP 160/100 — — — 100/80 Has residual symptoms

TABLE V—Continued

Name	Duration of Symptoms	Pertinent Findings	Operation	Result of Operation
46. Edward H. Lt. USNR Age 28	7 yrs.	Dyspnea, headaches, precordial pain on exertion, of 6 mos. duration. BP 160/110. Eyegrounds Grade I. Cardiovascular system normal. 2-step test positive. Urinary functions good. Positive cold pressor test	Bilat. thoracolumbar sympathectomy. T8—L1	Excellent. BP 118/80 — 130/90. Cold pressor test no longer positive. 2-step test not positive. Emotionally stable. No further precordial pain. 3 mos.
47. Charles C. W/O USN Age 41	2½ yrs.	BP 150/105 — 2 mos. morning headache and dyspnea on exertion. Eyegrounds Grade II. Heart slightly enlarged with fullness L. ventricle by roentgen-ray. ECG compatiable with hypertension. Renal function good. Abnormal cold pressor test	Bilat. thoracolumbar sympathectomy T8—L2.	BP 130/90 — 140/98. Relieved of all symptoms. 2 mos.
48. Joseph F. MM3c Age 22	4 mos.	Severe frontal headaches. BP 160/110 — 180/120. Eyegrounds within normal limits. Cardiovascular system normal. Renal function good. ECG within normal limits. Abnormal cold pressor test. Good sedation test	Bilat. thoracolumbar sympathectomy T8—L2.	BP 110/82 — 120/88. Relieved of all symptoms. 2 mos.
49. Barclay W. Lt. USN Age 27	4 mos.	Severe occipital headaches. Fundi Grade II. Cardiovascular workup neg. ECG, L. axis deviation. Blood chem. normal. Urinary function good. Abnormal cold pressor test. BP 150/100 — 180/130	Bilat. thoracolumbar sympathectomy. T10—L1	Free from headaches. Feels well. BP 130/100 — 1 yr. later. Returned to duty in Pay Corps, but BP 160/110 — 185/130 — 2 yrs. later. Kidney biopsy showed Grade II hypertensive changes
50. William W. VAP Age 45	13 mos.	Residual signs of R. hemiplegia and recent L. hemiplegia. Heart enlarged, tortuous aorta by roentgen-ray. ECG abnormal. Urine alb., diminished ability to concentrate. Fundi Grade III. I-V pyelogram normal. BP 220/130 — 300/140 Bilat. Hoffman PSP 20% excretion	Bilat. thoracolumbar sympathectomy. T9—L2.	Lying BP 200/130 — Sitting BP 170/120. Standing 80—dizzy — 0—faint. No late follow-up. Biopsy kidney chr. vascular nephritis, Grade I
51. Robert R. Lt. USNR Age 35	6 mos.	6 mos. fatigue, headaches. 3 mos. visual blurring and nocturia 1 mo. Eyegrounds Grade IV. Convulsions with amnesia 1 mo. Normal pyelogram. Urine-alb.-diminished concentration power. ECG—coronary disease. Lumbar puncture inc. pressure without increased protein. BP 190/130 — 200/150. Markedly abnormal cold pressor test	Bilat. thoracolumbar sympathectomy. T8—L3.	Improvement in eyegrounds. Decreased CSF* pressure. BP 125/90 — 118/100. 14 mos. Fundi almost normal 2-step test indicative of coronary insufficiency

* Cerebrospinal fluid.

12-4-44: B/P.	Lying	Sitting	Standing	Ice water	Lying	Standing
	198/120	194/128	200/138		200/122–190/114	196/128
Pulse	96	88	100		88	96

Eyegrounds clear of exudate, hemorrhages or papilledema; moderate nicking.

12-5-44: Old incision reopened and carried up to rib 7. L2 and L3 ganglia removed. R10 then resected (5 cm.) T8, T9, T10 ganglia and 5 cm. of major splanchnic nerve resected. B/P. 130/80.

12-7-44: B/P. 190/110.

12-13-44: B/P. at former level

1-4-45: B/P. back to old level.

2-1-45: Well — B/P.	Lying	Sitting	Standing
	160/110	155/105	160/100

9-5-45: Reëxamination at U. S. N. H. St. Albans. Doing six hours work, six days a week at M. I. T.

B/P.	Lying	Sitting	Standing
	165/110	166/118	166/120

Fundi almost normal, minimal A-V nicking. Arteries slightly narrowed. Veins normal. Disk normal. No exudates or hemorrhages.

Cold pressor test — 154/120 to 160/115

Pulse 76 72

in striking contrast to previous test of 5-31-43 which was 200/140 to 300+/180.

Case 2.—Edward H., Lt. (jg) U.S.N.R. (Case 46).

This 29-year-old officer was known to have mild hypertension at the age of 22. When he started naval service in 1942, his B.P. was recorded as 148/98. In 1943, he was hospitalized for the complaint of precordial pain and his B.P. at that time was recorded as 176/100, falling to the level of 128/80 with bed rest. He was then returned to duty. When examined for promotion in June, 1945, it was ascertained that his B.P. was 170/112. At this examination, he complained of frequent headaches, mild dyspnea, irritability, and precordial pain with exertion. He was, therefore, hospitalized for further investigation. No familial history of hypertension was obtained.

Pertinent findings on physical examination: Grade I changes of the fundi were noted. The heart was not enlarged, a fact confirmed by cardiac fluoroscopy, and the sounds were of good quality, but A2 was accentuated. The B.P. averaged 174 systolic and 110 diastolic, with a fall to 114 systolic and 86 diastolic with the use of sodium amytal. Several cold pressor tests indicated a marked hyperreaction. A "Master"[10, 11] two-step test was reported to indicate a coronary insufficiency.

All laboratory data, including P.S.P., urea clearance, dilution and concentration tests, excretory urogram, and examinations of urinary sediment were considered within normal limits.

After sympathectomy the following changes were noted in addition to the patient's voluntary observations that he no longer had headache, dyspnea or precordial pain on effort: A "Master" two-step test, performed two months after operation, was considered normal, as was a cold pressor test. His systolic B.P. has not been noted to exceed 130 systolic and 86 diastolic. He considered his nervousness and irritability minimal.

This patient has been returned to full naval duty.

Discussion of Hypertension.—In this group of hypertensives, we are avoiding discussion at present for lack of long follow-up. It is apparent that in this small series, patients have been sufficiently relieved of symptoms so that they have become useful again and, in the case of Naval personnel, have returned to duty. Two cases are cited in detail. Unquestionably, this operation can set

back the hands of the clock for the majority of hypertensives under the age of 50, but whether even the most radical sympathectomy can permanently prevent the tendency for a late reëlevation of blood pressure we are not prepared to venture an opinion. Cases 44 and 41 have shown a tendency in this direction. The operation failed to produce a significant fall in blood pressure in only a single instance (Case 49), where the preoperative evaluation had predicted such a result. In Case 51, with an even more malignant form of hypertension but less organic arterial disease, operation has undoubtedly saved this officer from imminent death and has restored him to useful work for a period of over two years. Three patients have regained blood pressures that are essentially normal, and five that are in an intermediate range.

F. ANGINA PECTORIS

Methods of Study.—These patients were studied by the medical service and, when all efforts to obtain relief of severe cardiac pain by medication failed, they were considered candidates for surgery. As the medical examination showed that they were reasonably good surgical risks, resections of the upper thoracic ganglia on the side of the most severe pain was undertaken without hesitation. Excerpts of the case histories of these two patients are given in Table VI.

TABLE VI

ANGINA PECTORIS

Pt.	Presenting Symptoms	Duration of Symptoms	Pertinent Findings	Operation	Result of Operation
52. James T. VAP Age 44	Severe precordial pain radiating down left arm. Pain relieved only by morphine, not by nitroglycerine. Attacks occurred t.i.d.	3 yrs.—but severe 3 wks.	Obese, BP 142/100 ECG—abnormal. Heart not remarkable	L. thoracic ganglionectomy, T1—T3	Horner's syndrome left-sided, dryness. No angina, but warning symptom of epigastric constriction. 3 yrs.
53. Charles C. VAP Age 47	Unable to work since 1929 because of deep seated griping, precordial sensation brought on by exertion and poorly relieved by nitroglycerine. Pain most noticeable on right side of precordium radiating to right arm. Pain required morphine for relief	15 yrs.	BP 130/94 Heart not enlarged. Sounds indistinct, systolic murmur at apex. Anoxia test caused substernal pain. ECG showed coronary art. disease	R. thoracic ganglionectomy. Inferior cervical through T3	Completely free of pain on right side. Has not had to resort to morphine. 8 mos. later occ. has mild left-sided pain well controlled by ½ nitroglycerine. 4 yrs.

Discussion of Angina Pectoris.—It is self-evident that few cases of angina pectoris will appear in military personnel on active service. The condition is however, just as frequent in veterans as in civilian patients, and the veterans of the previous war are now entering the age-group of coronary disease. This group of patients is characterized by failure to obtain relief of pain by the usual medication or cardiac regimen; by the marked incapacity of the patient; by absence of cardiac failure or definite cardiac infarction.

In past experience with civilian patients one of us (J. C. W.) has treated 67 by paravertebral injection of 95 per cent alcohol around the upper three or four thoracic sympathetic ganglia, as compared with 74 in whom the corresponding ganglia were removed surgically. With either effective chemical or surgical destruction of these ganglia cardiac pain is abolished. Accurate infiltration of alcohol is more difficult and may be followed by a disagreeable intercostal neuralgia, and it should be reserved for those patients in whom advanced coronary disease or myocardial failure make the surgical approach too dangerous. With present day improvements in the selection of these patients, the advantages of intratracheal ether anesthesia and operation in the sitting position, the proportion that cannot safely be submitted to sympathectomy is steadily decreasing. There has been no report of death attributable to the removal of pain in coronary disease and a vast amount of suffering can be relieved by the coöperation of the cardiologist with the surgeon in suitable cases.

RESULTS AND CONCLUSIONS

In civilian life the Raynaud's syndrome, hyperhydrosis, and hypertension are often encountered in unstable, emotional individuals, or in those having high vasomotor tone. Psychologic experiences in military life accentuate these phenomena, and the transition from military to civilian life, in turn, may evoke similar responses.

In summary, the results of preganglionic sympathectomy for increasing circulation in Raynaud's syndrome (short of pallid asphyxia), as well as in thromboangiitis obliterans, arteriosclerosis and vascular complications with associated vasoconstriction have been uniformly good. The same is true in hyperhydrosis and in painful states such as causalgia, certain amputation stump neuralgias, and angina pectoris. Our conclusions in hypertension are limited, due to lack of long follow-up, but the immediate results of those observed in a two-year follow-up are: significant lowering of blood pressure; relief of distressing headaches, nervousness and irritability; and the rehabilitation to useful occupations. No fatalities or serious complications have resulted from our operative procedures thus far.

REFERENCES

1 Allen, E. V., and Brown, G. E.: Raynaud's Disease: A Critical Review of Minimal Requisites for Diagnosis. Am. J. Med. Sc., **183**, 187–200, 1932.

2 Bigger, I. A.: Treatment of Traumatic Aneurysms and Arteriovenous Fisulas. Arch. of Surg., **49**, 170–178, 1944.

3 Crutcher, R. R.: Sympathectomy for Ischemia following Femoral Artery Ligation. ANNALS OF SURGERY, **123**, 304–310, 1946.

4 Doupe, J., Cullen, C. H., and Chance, G. Q.: Posttraumatic Pain and Causalgic Syndrome. J. Neurol., Neurosurg. and Psychiat., **7**, 33–48, 1944.

5 Granit, R., Lessell, L., and Skoglund, C. R.: Fiber Interaction in Injured or Compressed Region of Nerve. Brain, **67**, 125–140, 1944.

6 Hines, E. A., and Christenson, N. A.: Raynaud's Disease among Men. J. A. M. A., **129**, 1–4, 1945.

7 Hines, E. A. Jr.: Technic of the Cold Pressor Test. Proc. Staff Meetings, Mayo Clinic, **14**, 185–187, 1939.

[8] Katz, B., and Schmitt, O. H.: Electric Interaction between Two Adjacent Nerve Fibers. J. Physiol., **97,** 471–488, 1940.

[9] Keith, N. M., Wagener, H. P., and Barker, N. W.: Some Different Types of Essential Hypertension: Their Course and Prognosis. Am. J. Med. Sc., **197,** 332, 1939

[10] Master, A. M., and Oppenheim, E. T.: A Simple Exercise Tolerance Test for Circulatory Efficiency. With Standard Tables for Normal Individuals. Am. J. Med. Sc., **177,** 223, 1929.

[11] Master, A. M., Friedman, R., and Dock, A.: The Electrocardiogram after Standard Exercise as a Functional Test of the Heart. Am. Heart J., **24,** 244: 777, 1942.

[12] Minor, V., Dtsch. Z. Nervenheilk, **101,** 302–308, 1928.

[13] Mitchell, W. W., Morehouse, G. R., and Keen, W. W.: Gunshot Wounds and other Injuries of the Nerves. J. B. Lippincott Co., Phila., 1864.

[14] Montgomery, H.: Am. Heart Assn., Vol. 13, No. 9.

[15] Richter, C. P., and Woodruff, B. G.: Changes Produced by Sympathectomy in the Electrical Resistance of the Skin. Surgery, **1,** 957–970, 1941.

[16] Rose, A. C., Hess, N. O., and Welch, S. C.: Vascular Injuries of the Extremities in Battle Casualties. ANNALS OF SURGERY, **123,** 2, 1946.

[17] Smithwick, R. H., and White, J. C.: Peripheral Nerve Block in Obliterative Vascular Disease of the Lower Extremity. S. G. & O., **60,** 1106, 1935.

[18] White, J. C., and Smithwick, R. H.: The Autonomic Nervous System: Anatomy, Physiology and Surgical Application, 2nd Edition, The Macmillan Co., N. Y., 1941.

[19] White, J. C.: Pain following Injuries of Peripheral Nerves. U. S. Naval Medical Bull., **45,** 5, 1945.

GRANULAR CELL MYOBLASTOMA OF THE MAMMARY GLAND*

C. D. Haagensen, M.D., and Arthur Purdy Stout, M.D.

New York, N. Y.

*From the Surgical Pathology Laboratory of the College of Physicians and Surgeons, Columbia University, and the Department of Surgery, Presbyterian Hospital, New York, N. Y.

Although granular cell myoblastoma is most commonly seen in the tongue, this interesting neoplasm may occur almost anywhere in the body and at any age. In addition to two of these lesions that we have encountered in the skin over the breast region, we have observed five in the mammary gland itself. In this situation this lesion must be distinguished from carcinoma, which it closely resembles. Since granular cell myoblastoma in the breast appears to be benign, requiring only local excision, the differential diagnosis is an important one.

We shall describe our five cases in detail, because they illustrate certain features which may be of aid in the diagnosis of myoblastoma of the breast.

CASE REPORTS

Case 1.—S. P. Unit No. 666228: A Russian woman, age 30, was admitted to the Presbyterian Hospital in August, 1930, for secondary anemia, hemorrhoids, fever of undetermined origin, and obesity. Examination of the breasts at the time did not reveal anything abnormal. Her hemorrhoids were operated upon.

In November, 1931, she discovered a lump in her left breast while palpating it after reading a pamphlet on cancer. Examination showed a hard 1.5-cm. tumor situated in the inner sector of the breast over the 4th interspace 2 cm. from the edge of the sternum. There was no distortion of the contour of the breast and no dimpling of the overlying skin. The tumor was freely movable over the underlying chest wall. There were no enlarged axillary lymph nodes.

On November 16, 1931, under general anesthesia, the lesion was excised. The cut-surface of the tumor was white and opaque. Its edge was not clearly demarcated from the surrounding fat, although it had a lobulated character. A frozen-section was made and it was decided that the lesion was a benign one. The wound healed without incident.

Microscopic.—The tumor was composed of cells with small ovoid nuclei and large finely granular cytoplasms. There were irregular coarse collagenous septa among them, but most of the cells lay in immediate contact one with another. The scharlach R stain failed to show lipoid in the cells. The tumor had no capsule. Its structure was clearly that of a granular cell myoblastoma.

Follow-up.—The patient was last seen September 26, 1945, 13 years and 10 months after her breast operation. There had been no recurrence of the tumor.

Case 2.—A. M., Unit No. 373338: An American Negress, age 19, came to the Presbyterian Hospital first in March, 1933. In January, 1932, her first pregnancy had terminated in cesarian section at another hospital. Four weeks following delivery she had had an abscess in her left breast. It was incised and drained for some time.

Examination revealed an oblique scar of the former abscess in the radius of 11 o'clock just outside the areola in the left breast. The breast was slightly smaller than the right one, but contained no tumor. The patient was found to have syphilis and was given antisyphilitic treatment. She shortly became pregnant again, and was delivered for the second time by cesarian section in May, 1934. A third pregnancy occurred the following year, and was terminated by cesarian section in May, 1935. At this time she was sterilized.

In July, 1937, at the age of 24, she came to the clinic complaining of a tumor in the left breast. She had had no trouble with this breast since the abscess in it in 1933. Previous examiners had not noted any tumor in it.

Examination now showed a firm tumor, measuring 2.5 x 1 x 0.5 cm. in the upper inner part of the left breast. It lay over the second interspace close to the sternal edge. The skin could be moved freely over it, but the tumor seemed to be somewhat attached to the underlying chest wall. On August 9, 1937, under local anesthesia with novocaine, the lesion was biopsied. It lay in breast tissue and was not encapsulated. It was adherent to the pectoral fascia. The whole lesion was removed. On section, the tumor was firm, fibrotic, and grayish-yellow. The wound healed well.

Microscopic.—The lesion was made up of cells with small nuclei and voluminous cytoplasms filled with fine granules. There were no vacuoles, and the scharlach R stain failed to show lipoid. The lesion was a characteristic granular cell myoblastoma. It had no capsule, and infiltrated the adjacent breast tissue.

Follow-up.—The patient was last seen on October 30, 1945, eight years and two months after operation. There was no recurrence.

Case 3.—L. J., Unit No. 714878: A West Indian Negress, age 37, came to the Presbyterian Hospital, July 12, 1943, complaining that she had had a tumor in the right breast for seven years. She recalled striking her chest against the corner of a table at that time. There was no subsequent ecchymosis, but a few days after the blow she noted the tumor for the first time. It had not changed appreciably in size during the following seven years. It had never been painful nor tender.

Examination showed a hard, rather well-circumscribed tumor lying over the fourth right interspace close to the edge of the sternum. It measured 1.5 cm. in diameter. Although no dimpling of the overlying skin could be demonstrated, the tumor was fixed, to an abnormal degree, to the underlying pectoral fascia, for when the pectoral muscles were contracted with the patient sitting upright the tumor and the breast tissue around it were pulled upwards sharply. No such elevation of the corresponding part of the left breast could be demonstrated. When the patient lay in the supine position contraction of the right pectorals markedly limited the movability of the tumor over the chest wall. There was no distortion of the contour of the right breast, and the right nipple and areola were normal.

On November 18, 1943, under avertin, gas and oxygen anesthesia, operation was undertaken. All preparations had been made for a radical mastectomy should it prove to be necessary. A short incision was made directly over the tumor and a small wedge, measuring 2 x 10 mm., was excised from the surface of the lesion after careful hemostasis. Frozen-section revealed that it was a granular cell myoblastoma. The whole tumor was, therefore, excised. Its cut-surface was finely granular, and grayish-white with a tinge of yellow. Its edge was sharply defined from the surrounding fat (Fig. 1). The wound was closed with subcuticular and skin sutures of silk. Healing was uneventful.

Microscopic.—The tumor lay in mammary tissue, and had no true capsule. It was made up of rather large cells, with finely granular cytoplasms and small regular nuclei, lying in masses and strands in a fairly well developed collagenous stroma. The scharlach R stain did not show any lipoid in these cells. The tumor was clearly a granular cell myoblastoma.

Follow-up.—The patient was last seen October 8, 1945, just short of two years following operation. There was no evidence of recurrence.

Case 4.—Unit No. 739836: A Russian born Jewess, first came to the Presbyterian Hospital in 1928, when she was 47 years of age. She was found to have hypertensive cardiovascular disease, and mild diabetes, which was controlled without insulin. In 1930, she developed chronic tonsillitis, and tonsillectomy was done without incident. She failed to follow her diet and gained a good deal of weight as the years went by. In 1935, she was

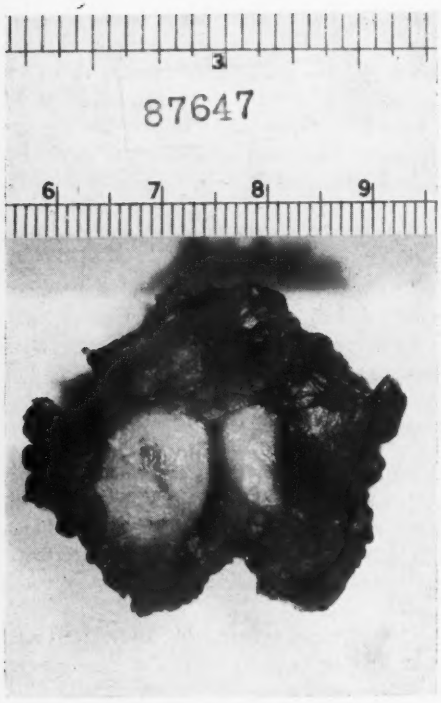


FIG. 1.—Gross appearance of myoblastoma of the breast (Case 3).

given insulin, but, by 1938, she was having so much trouble with her diabetes that she had to be hospitalized for a while. Protamine insulin controlled the diabetes, but as time went on she developed evidence of a considerable degree of coronary sclerosis.

In February, 1944, at the age of 63, she discovered a tumor in her left breast. It presented on the inferior aspect of the large dependent breast just cephalad to the inframammary fold. It was, therefore, concealed when the patient sat erect and in this position the only evident abnormality was slight elevation of the breast (Fig. 2). It was very evident with the patient in the supine position, however, as a projecting tumor situated over the fifth interspace half way between the sternal edge and the nipple line (Fig. 3). It was very hard, and measured 4 cm. in diameter. The tumor and the breast tissue in which it lay were relatively fixed to the underlying chest wall. When the breast was pushed medially toward the tumor a definite dimple appeared in the skin over it. No enlarged axillary nodes were detected.

A presumptive diagnosis of carcinoma of the breast was made and all preparations completed for a radical mastectomy. Fortunately, a biopsy was done, a small wedge being removed from the surface of the lesion for frozen section. The only feature of the gross appearance that suggested something unusual was the fact that the cut-surface of the tumor was whiter than most carcinomas (Fig. 4). When the frozen section revealed that the lesion was a granular cell myoblastoma it was excised locally and the wound closed. Healing was uneventful.

Microscopic.—The tumor was made up of myoblasts with small oval nuclei and large finely granular cytoplasms (Fig. 5). The cells lay in solid masses and strands, often in immediate contact with one another without any intervening collagenous reticulum. The scharlach R stain failed to show any lipoid in the cells. The edge of the lesion was sharply defined against the adjacent mammary tissue, but there was no true capsule.

Follow-up.—The patient had had no recurrence of her myoblastoma when she was last examined on March 19, 1946, two years following operation.

The fifth case was observed by one of us (C. D. H.) at the Memorial Hospital some years ago. At that time the lesion was classified as a primary *xanthoma* of the breast, and it was reported under that name in 1932. At the time we did not know that, in 1926, Abrikossoff had traced the histogenesis of these tumors to muscle cells and named them "myoblastic myomas." When we came to realize the correctness of Abrikossoff's view of the origin of these tumors, restudy of this tumor of the breast left no doubt in our minds that it was a typical granular cell myoblastoma.

Case 5.—C. B. T., an unmarried Irish woman, age 74, was referred to Dr. James Duffy at the Memorial Hospital for treatment, August 7, 1930.

FIG. 2

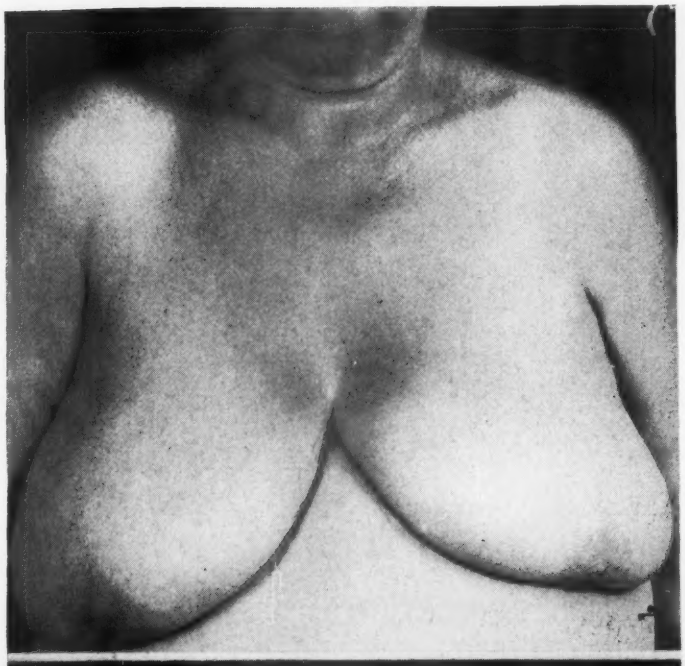


FIG. 3

FIG. 2.—Elevation of the breast caused by myoblastoma (Case 4).
FIG. 3.—Myoblastoma projecting from the breast, as seen in contour with the patient lying supine (Case 4).

Five years previously, about 1925, she had first observed a small lump in the inner portion of her left breast. It had grown very slowly. She had had no pain in it. Examination showed a large tumor in the upper inner quadrant of her right breast (Fig. 6). It measured 9 cm. in diameter and was elevated 4 cm. above the surface of the breast. The skin over it was reddened and shiny. The middle of the tumor was soft, suggesting a central area of necrosis. It was slightly movable over the underlying chest wall. The nipple was not retracted. There were no nodes palpable in the right axilla or supraclavicular space. In the left axilla several small soft nodes were felt. A clinical diagnosis of carcinoma of the breast with impending ulceration was made.

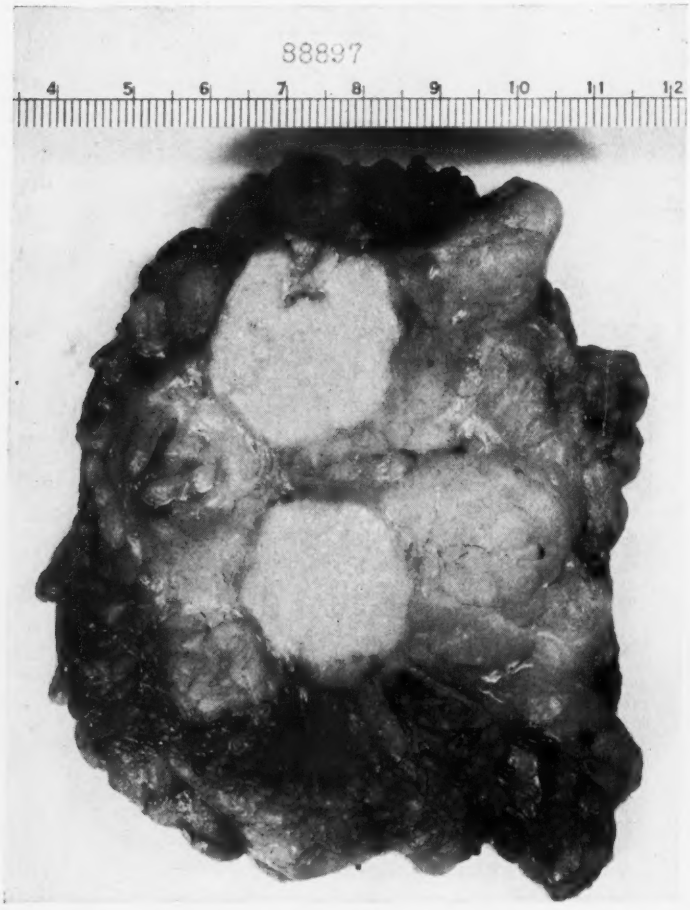


FIG. 4.—Gross appearance of myoblastoma of the breast (Case 4).

The patient was found to have, in addition, diabetes and chronic nephritis. It was, therefore, decided by Doctor Duffy that interstitial radiation would be the best treatment. Accordingly, August 26, 1930, steel needles containing a total of 85 millicuries of radon filtered by 0.3 mm. of gold and 0.2 mm. of steel were inserted into the breast and a total of 7,200 millicurie hours given. A reaction, limited to reddening and slight desquamation of the skin over the tumor, developed during the following weeks. The tumor decreased markedly in size during this period. By March, 1931, seven months after treatment, the

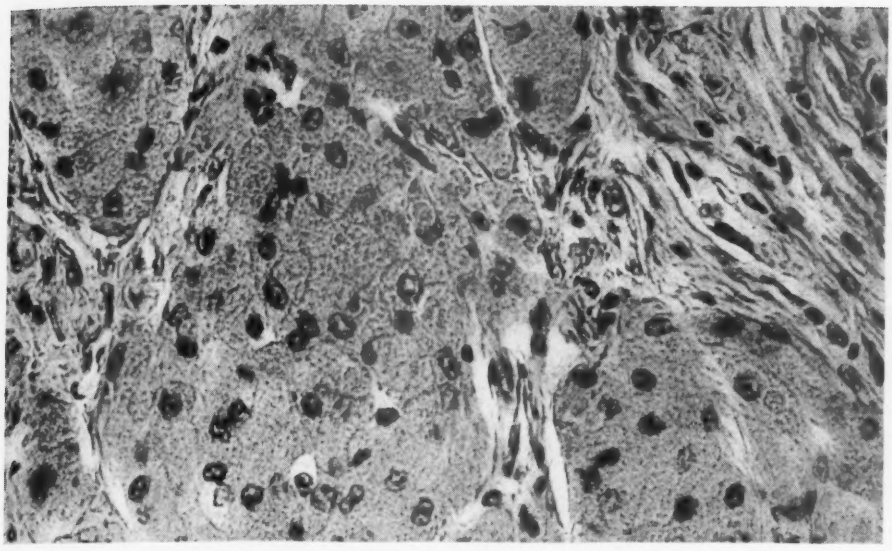


FIG. 5.—Microscopic appearance of myoblastoma of the breast (Case 4).

FIG. 6.—Myoblastoma of the upper inner sector of the breast (Case 5).

contour of the breast was almost normal. The reddish discoloration of the skin had completely disappeared. Of the tumor, only an indefinite area of induration in the breast tissue remained. It was decided that although there had been remarkable regression, a residuum of the tumor persisted. Since the diabetes had been brought under control and was no longer a contraindication to operation, a simple mastectomy, under local infiltration anesthesia with novocaine, was carried out on June 2, 1931. The tumor appeared to be encapsulated, and measured 6 x 4 x 6 cm. Its cut-surface was soft, reddish, and granular. Recovery was uneventful.

Microscopic.—The tumor was composed of large, round or polyhedral pale cells lying in the interstices of a rather prominent fibrous stroma. The cytoplasms of the tumor cells were finely granular or vacuolated. The nuclei were small and dark. Large portions of the tumor were necrotic: in these only degenerating tumor cells and amorphous débris remained. A sudan III stain showed droplets of the dye in the cytoplasms of some of the tumor cells. The tumor is a granular cell myoblastoma in which there has been a good deal of degeneration.

Follow-up.—One year after operation there had been no recurrence of the tumor.

We have been able to find but five previous reports of granular cell myoblastoma of the breast. All of them lack details. These reports follow:

Cheatle, writing in 1931, mentioned a "single solid tumour in the breast of a woman, age 38." It was circumscribed but not encapsulated, and the cut-surface had a characteristic (*sic*) yellow appearance. He classified it as a *xanthoma*. No follow-up was mentioned.

Abrikossoff, reported an undoubted case in his 1931 paper. His patient (No. 4 in his series) Mrs. V., was a Jewess, age 55, the wife of a physician. She was admitted, November 26, 1927, for a tumor of the left breast. She had had a cholecystectomy 16 years previously, and was a diabetic. She had noticed the tumor in her left breast two months previously. At that time it was a small firm nodule. It grew slowly, and was painless.

Examination showed a firm, well circumscribed, movable, hazel nut-sized tumor, situated in the upper outer sector of the left breast. The tumor was not adherent to the skin. The breasts were of average size and dependent.

On November 28, 1927, the tumor was excised. It was a rounded nodule, 2 x 1.5 cm., very firm, light gray in color, and with a somewhat fibrous cut-surface. Microscopic examination showed it to be a granular cell myoblastoma.

No follow-up was included.

Meyer described another myoblastoma of the breast in 1932. The tumor (No. 2 in his series) was removed from the breast of a three-months pregnant woman on December 8, 1931. It was the size of a peanut, was rather well-circumscribed, and lay close beneath the skin over the breast. It penetrated the glandular tissue of the breast, but did not extend down to the pectoral muscle. The wound healed primarily. Microscopic examination showed the lesion to be a granular cell myoblastoma. There had been no recurrence six and one-half months later.

Geschickter mentioned myoblastoma of the breast in his 1934 paper on tumors of muscle. He stated that he had observed three myoblastomas of the breast, and included a photograph of the gross specimen of one (Path. No. 39034). This lesion was said to be firm and encapsulated. Its location in the

breast was not stated. There was no follow-up. No details regarding the other presumed cases were presented.

Gray and Gruenfeld reported a myoblastoma of the breast in 1937. In their case (No. 5 in their series) no clinical details were available, except that the large encapsulated tumor was removed from the breast of a white woman, in the Out-patient Department. The tumor measured about 10 cm. in diameter, had a grayish color and a firm consistency. Microscopic examination showed it to be a typical granular cell myoblastoma. There was no follow-up.

Discussion.—The granular cell myoblastoma of the breast is, so far as experience goes, a benign tumor. It is impossible to ignore the fact that this tumor type may on occasion become malignant and metastasize as has been pointed out by Ravich, Stout and Ravich, but this is probably such an uncommon event that it is justifiable to treat the tumor as benign when it is encountered. In the breast its greatest importance depends probably upon the fact that it may closely simulate carcinoma of the breast. Unless the surgeon and pathologist are aware of this similarity myoblastoma may be mistaken for carcinoma and the breast needlessly sacrificed.

It is apparent from our five cases that myoblastoma occurring in the breast can produce all of the clinical signs of early carcinoma. The lesion is hard. It is relatively fixed in the breast tissue surrounding it. It may be abnormally attached to the underlying pectoral fascia. It may cause dimpling of the overlying skin. The gross appearance of the lesion is enough like carcinoma to betray most pathologists into making this diagnosis if they depend upon the gross appearance alone, without taking the precaution of making a frozen-section. The closest scrutiny will show that myoblastoma is more sharply circumscribed than most carcinomas, and that its cut-surface is whiter and more uniform than the grayish chalk-streaked surface of the typical carcinoma. These differences, however, are slight and easily missed.

We have made it a practice to make immediate frozen-sections of all lesions removed for biopsy from the breast, because of the similarity in gross appearance of myoblastoma, and several other benign lesions that occur in the breast, to carcinoma. Myoblastoma is easily recognizable in a good frozen-section. In our two most recent cases, Nos. 3 and 4, the diagnosis was made in this way. We do not use the aspiration method of biopsy in the diagnosis of breast lesions, for we have found it to be unreliable.

The source of the muscle cells from which these myoblastomas arise in the breast is an intriguing, although perhaps a somewhat theoretical question. Abrikossoff traced the origin of these tumors to striated muscle, and the fact that their most common site is the muscular substance of the tongue supports this concept. But as our knowledge of the myoblastomas has developed it has become obvious that they sometimes occur in regions of the body where there is no muscle tissue of any sort. The gum of the newborn infant is a good example. We have observed three granular cell myoblastomas in this location, and there are reports of several similar cases.

The breast is likewise without muscle tissue, except for a network of smooth

muscle fibers in the subareolar region and in the nipple, and encircling the terminal ducts beneath the nipple. Seitz made a special study of the musculature of the breast and concluded that there is no striated muscle tissue in the breast proper. A diagram showing the location of our four myoblastomas (Fig. 7) makes it clear that the tumors were all in the periphery of the breast far from the areolar and nipple region.

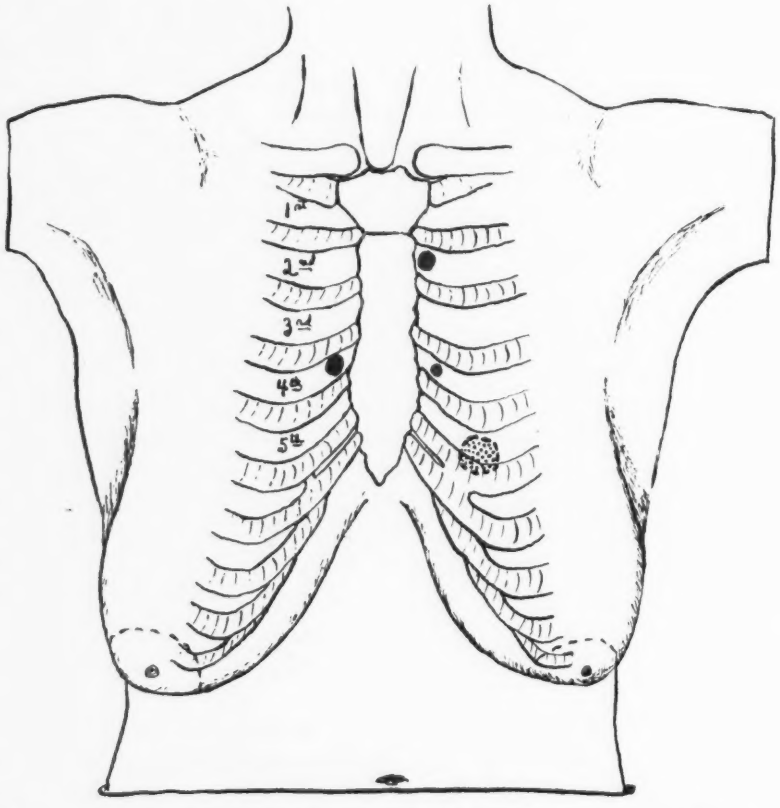


FIG. 7.—Diagram showing the location, in relation to the sternum and intercostal spaces, of the myoblastomas in Cases 1, 2, 3, and 4.

Our search for muscle tissue from which these tumors might have developed, therefore, turns to the musculature of the chest wall. All four of our tumors appeared to have developed within the breast itself superficial to the pectoral fascia, and, therefore, superficial to the pectoralis major muscle.

The occurrence of these myoblastomas adjacent to the sternum suggests a possible origin from the *sternal* muscle, a small anomalous muscle of great variability which occurs in from 1 to 10 per cent of Europeans. Eisler describes this muscle as extending vertically or diagonally across the upper chest close to the sternum, superficial to the pectoral fascia.

Another possible origin is from the platysma. Its fibers extend in a fan-like manner down over the chest wall from the neck. They may, according to Eisler, extend as far caudally as the fourth rib. These muscle fibers lie upon the superficial fascia and are, therefore, immediately adjacent to the mammary gland which lies beneath this fascia.

It may be of diagnostic significance that all four of the granular cell myoblastomas of the breast that we have studied personally, and in which we know the exact site of the lesion, developed in the medial half of the breast. Until more cases have been reported we are not justified in concluding that these tumors do not occur in the lateral half of the breast, but the questions is worth bearing in mind.

SUMMARY

Five new cases of granular cell myoblastoma of the breast are described and the case reports of five previously reported cases reviewed.

The importance of these tumors comes from the fact that they closely simulate, in both their clinical characteristics and gross appearance, carcinoma of the breast. Biopsy and frozen-section are required to differentiate the two lesions.

REFERENCES

Abrikossoff, A. I.: Über Myome, ausgehend von der quergestreiften willkürlichen Muskulatur. Virchows Arch. f. path. Anat., **260**, 215, 1926.

Abrikossoff, A. I.: Weitere untersuchungen über Myoblastenmyome. Virchows Arch. f. path. Anat., **280**, 723, 1931.

Cheatle, Sir G. L., and Cutler, M.: Tumours of the Breast. Philadelphia, 1931, p. 307.

Eisler, P.: Die Muskeln des Stammes. In Bardeleben: Handbuch der Anatomie des Menschen, Vol. 2, Part 2, first section, page 109 (platysma) and page 471 (sternal muscle), Jena, 1912.

Geschickter, C. F.: Tumors of Muscle. Am. J. Cancer, **22**, 403, 1934.

Gray, S. H., and Gruenfeld, G. E.: Myoblastoma. Am. J. Cancer, **30**, 699, 1937.

Haagensen, C. D.: Xanthoma of the Breast. Am. J. Cancer, **16**, 1077, 1932.

Meyer, R.: Myoblastentumoren ("Myoblastenmyome" Abrikossoff). Virchows Arch. f. path. Anat., **287**, 55, 1932.

Ravich, A., Stout, A. P., and Ravich, R. A.: Malignant Granular Cell Myoblastoma Involving the Urinary Bladder. ANNALS OF SURGERY, **121**, 361, 1945.

Seitz, A.: In Halben-Seitz: Biologie und Pathologie des Weibes. Vol. 5, Part 2, page 1290. Berlin, 1925.

COMBINED ROENTGEN RADIATION AND SURGICAL TREATMENT OF LARGE BENIGN GIANT CELL TUMORS OF BONE

G. Edmund Haggart, M.D.,
DEPARTMENT OF BONE AND JOINT SURGERY

AND

Hugh F. Hare, M.D.,
DEPARTMENT OF RADIOLOGY
THE LAHEY CLINIC
Boston, Massachusetts

In the voluminous literature about benign giant cell tumor of bone the reader is frequently cautioned against the combination of radiation therapy and surgery in the management of this tumor. The reason appears to be that radiation therapy would jeopardize the process of tissue repair. On the basis of our experience, we believe this concept to be erroneous. It is, therefore, the purpose of this paper to present the therapeutic technic and results obtained in the management of seven patients with proven diagnoses of benign giant cell tumor of bone which presented difficult problems in treatment. The treatment entailed a combination of roentgen radiation which was followed by surgery comprising removal of the tumor with thorough curettage and then filling the defect with bone grafts. Neither chemical nor thermal cauterization was employed.

In those benign giant cell tumors of bone which are readily accessible and can be removed without sacrifice of function, we believe in immediate and complete excision. Examples of such tumors are those observed in the vertebral spinous and transverse processes.

In 1936, the first patient was treated by the combination of preoperative roentgen radiation followed by surgery, and the results were so satisfactory that when three years later we were consulted by a young woman, age 26, who had been advised amputation because of an unusually large, rapidly-growing benign giant cell tumor in the lower end of the femur, the same procedure was adopted with a satisfactory result.

The remaining five cases exhibit varied clinical aspects of the same condition, and were treated in a similar manner.

RADIATION THERAPY

All of the patients in this group have received approximately (details in case reports) 1,800 r, measured in air, delivered through two portals using 200 K.V.P., 1 mm. of copper filtration, 50 cm. distance, and a cone large enough to more than cover the lesion, to deliver a total dose of 900 r measured in air to each skin area. This quantity of radiation when properly filtered and given in divided doses is not enough to produce skin or tissue changes, yet is adequate to temporarily arrest the growth of the tumor and to allow cortical healing.

Roentgenograms taken in the first four to six weeks following radiation treatment usually reveal further bone atrophy and apparent progression of the tumor, but in eight to ten weeks following radiation, beginning appearance of calcium deposits is evident, plus replacement and thickening of the cortex. Also, if there originally was protrusion of the tumor into the soft tissue, this mass is diminished in size. In eight to 12 weeks after radiation, bone cortex is again intact and sufficiently developed to permit thorough curettage and removal of the tumor tissue.

Postoperative roentgen radiation has not been given except in one patient (Case 4), a 58-year-old laborer, who had a large tumor of the upper end of the tibia, in whom the operation was planned in two stages because of his extremely poor physical condition. Following the first stage, comprising very thorough curettage and removal of the tumor tissue, it was later considered unwise to again submit him to surgery and this man was, therefore, given additional roentgen radiation.

OPERATIVE PROCEDURE

The affected area of the bone is exposed and a window cut in the cortex of minimal size consistent with thorough visualization of the cavity. Tumor tissue is then carefully and very thoroughly curetted out. Every effort is made to protect the cartilage of the joint. The cavity is next tightly packed with bone grafts which have meanwhile been removed from the tibiae and/or ilium. Thereafter, the fibrous envelope which had previously been dissected off the area where the window was cut is carefully approximated with chromic sutures and the remainder of the wound closed in layers and a plaster encasement applied of an extent sufficient to adequately support the extremity, as for example, when the lower end of the femur is involved, a hip spica. In one patient (Case 7), the operation advocated by Codman was employed as a final procedure, removing a considerable portion of the wall of the cavity and leaving a flap of periosteum on the concave side of the bone defect.

In comparison with surgery on similar cases who did not receive preoperative radiation therapy, the operator has been much impressed by the relative avascular character of the tumor tissue in this group of patients. Furthermore, the tumor is comparatively firm as opposed to the usual friable tissue removed when radiation is not employed. The technical details of the curettage are thereby rendered simpler and we believe the surgeon is much less apt to leave bits of tumor tissue behind.

REPORT OF CASES

Case 1.—This 40-year-old paper mill employe was admitted, June 24, 1936, because of pain and marked disability in relation to the left knee, of four months' duration. Roentgenograms on admission (Fig. 1) revealed a tumor of the distal left femur and at one point there was evidence that the process had broken through the cortex.

Preoperative roentgen ray treatment was given from July 28 to July 31, 1936, using the following factors: 200 K. V. P., 50 cm. distance, 1 mm. of copper and 1 mm. of

aluminum filtration, port 15 cm., round cone, giving a daily dose of 400 r measured in air. Four treatments were given for a total of 1,600 r.

At operation, August 3, 1936, the frozen-section diagnosis was benign giant cell tumor of bone, which was confirmed on the permanent section. Thorough curettage and removal of the tumor tissue was performed, no cauterization, and the cavity then packed with bone grafts removed from the right tibia. The wound healed by first intention.

The patient was last examined October 1, 1945. Figure 2 exhibits excellent recalcification of the lateral condyle of the femur and the contour thereof was fairly normal. There was no evidence of recurrence. Roentgenograms of the lungs were negative. He had no disability in relation to the knee, and there were no changes in the skin.

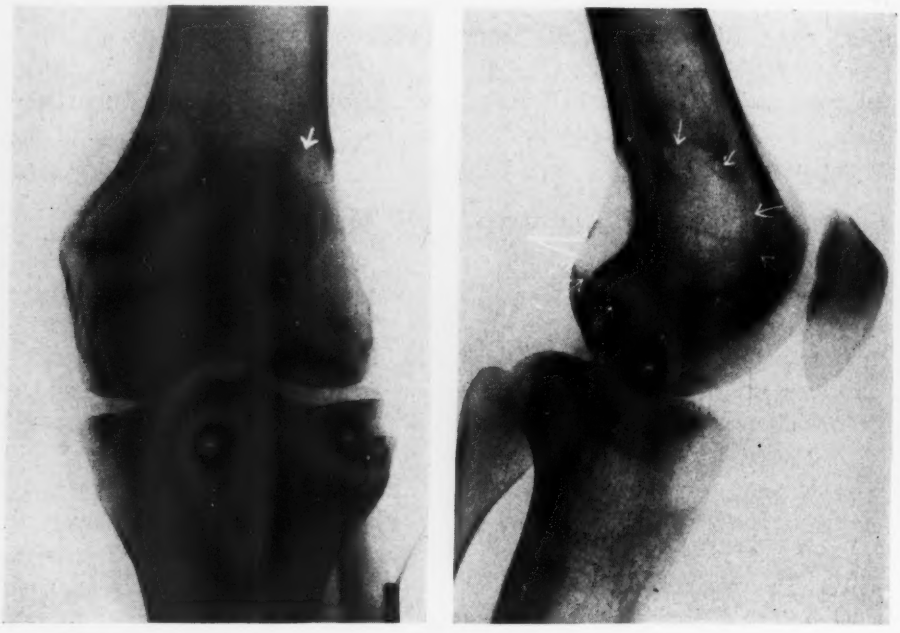


FIG. 1.—(Case 1): Preoperative roentgenogram revealing benign giant cell tumor involving the lower aspect of the femur. Symptoms of four months' duration. Complete disability on admission.

Case 2.—A 26-year-old girl student was admitted to the Clinic, January 10, 1939, with a two and one-half-year history of pain and disability in relation to the left knee region. She was operated upon elsewhere in 1936 because of a presumed internal derangement, and one of the semilunar cartilages removed. She did not improve. Finally, in October, 1936, a definite soft-tissue swelling appeared in the vicinity of the knee. It was found to involve the bone on roentgenologic examination. A biopsy was performed elsewhere. The pathologic report was giant cell sarcoma (this slide was obtained prior to the patient's admission and gone over by Dr. Shields Warren who reported benign giant cell tumor of bone without any evidence whatsover of malignancy).

Throughout 1937 and 1938 she was disabled, wearing a plaster encasement much of the time, and had been in bed continuously since October, 1938. During this interval following the surgery she had roentgen ray treatments, also given elsewhere, details not known. In addition, during this period she apparently experienced two pathologic fractures. Because amputation had been advised, the patient came to the Clinic for another opinion.

Roentgenologic findings on admission were those as shown in Figure 3. The leg, protected in an encasement, was markedly thickened and swollen throughout, especially around the region of the knee, with evidence of postradiation changes in the skin. There was marked pain in the distal thigh and knee region, and inability to move the knee joint. The patient appeared to be in excellent general condition. Roentgenograms of the lung were negative.

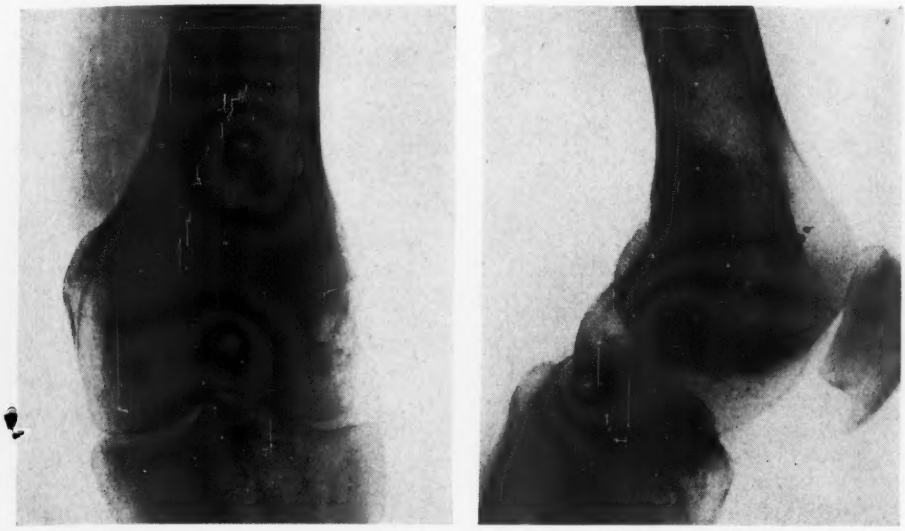


FIG. 2.—(Case 1): Anterior and posterior roentgenograms nine years and eight months after operation. Note recalcification of the lateral condyle of the femur and a relatively normal contour, with no evidence of recurrence of tumor. Normal function of knee joint.

In view of the definite assurance this was a benign lesion, we felt every effort should be made to save the extremity. An exhaustive study of various possible methods of surgical treatment was made. In view of the size of the tumor and the fact that an appreciable portion of its periphery did not exhibit any cortex, and especially because it was felt that supplementary roentgen radiation would aid in recalcifying and limiting the lesion, it was decided to carry out initial intensive roentgen ray treatment, to be then followed by surgical excision of the tumor tissue, preservation of as much of the cortex as possible, and filling the area with bone transplanted from elsewhere in the body. Therefore, the patient received a total of 1,800 r through two portals, using the same factors employed in the preceding case. There was pronounced increase in the calcification and apparent beginning repair of the tumor area (Fig. 4).

Operation was performed, May 18, 1939, when the entire cavity was thoroughly and carefully curetted. Cauterization was not employed, and the cavity was filled with bone grafts transplanted from both tibiae. Convalescence was uneventful following surgery and the wound healed by first intention. By September 19, 1939, she had progressed to walking in a supporting caliper and the roentgenograms showed progressive fusion of the bone grafts (Fig. 5).

On February 14, 1940, a small defect was observed on the anterior surface, about 4 cm. above the patella, which had not previously been noted. It was the opinion of the roentgenologist (H. F. H.) this should be treated by radon seeds, which was carried out on March 14, 1940.

The roentgenograms taken on February 21, 1946 (Fig. 6), indicate a healed lesion and no evidence of recurrence. The patient clinically is well, active, working full-time

and the only disability is that occasioned by limitation of knee motion which had been accepted as inevitable when first seen, due to deformity of the articular cartilage. Post-radiation skin pigmentation is evident but no other abnormality.

Case 3.—This 42-year-old clerk was admitted, October 20, 1939, because of persistent soreness and discomfort in the left ankle region of six months' duration, initiated by two episodes of spraining the ankle. There was persistent swelling, becoming very marked if she was on her feet for any length of time. The general condition of the patient was

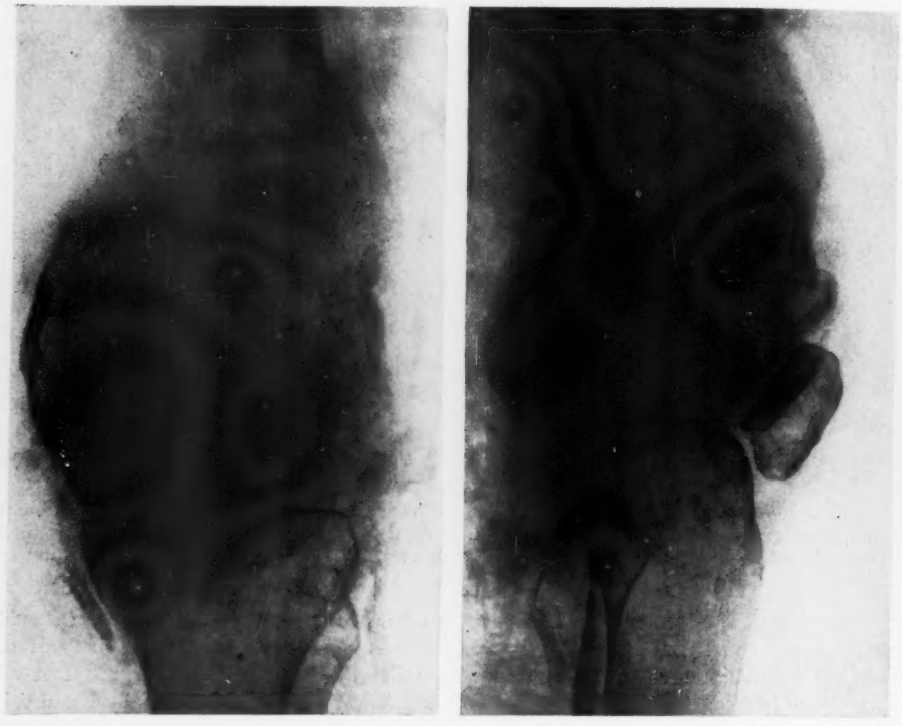


FIG. 3.—(Case 2) : Preoperative roentgenogram of a rapidly growing benign giant cell tumor of the lower end of the femur. Note absence of cortex over an appreciable part of the lesion and the irregularity of the articular cartilage of the femur.

excellent. The admission roentgenograms (Fig. 7) indicated a benign giant cell tumor. The patient was, therefore, started on roentgen radiation treatment, receiving a total of 1,500 r to each of two lateral portals, using the same factors as previously described, except for a 10 cm. cone.

At operation, January 22, 1940, the tumor mass was found to occupy the anterior and lateral three-fourths of the lower end of the tibia, but had broken through into the soft tissues, especially in the vicinity of the lateral malleolus and extended down alongside of but not into the ankle joint. The tumor tissue was carefully curetted out, no cauterization done, and the area packed with bone fragments removed from the right tibia. The wound healed by first intention. The patient was discharged as ambulatory, with crutches, from the hospital February 18, 1940.

The last physical examination and roentgenologic observations were obtained on February 7, 1945, at which time she presented a normal appearing ankle, no visible skin changes, with no swelling, normal motion of the joint and no symptoms. The roentgenograms (Fig. 8) exhibit no evidence of recurrence of the tumor.

Case 4.—This 58-year-old laborer was admitted to the Clinic, May 17, 1943, because of pain in the region of the left knee, of two years' duration. In 1941, he had been operated upon elsewhere for removal of the tumor in the region of this left knee which the family understood was not malignant. Within six months' time symptoms began to recur, had progressively become more marked, and on admission he showed marked disability in relation to the left lower extremity, with pronounced muscle atrophy and a 70-degree flexion contracture of the left knee joint. His general condition was not favor-

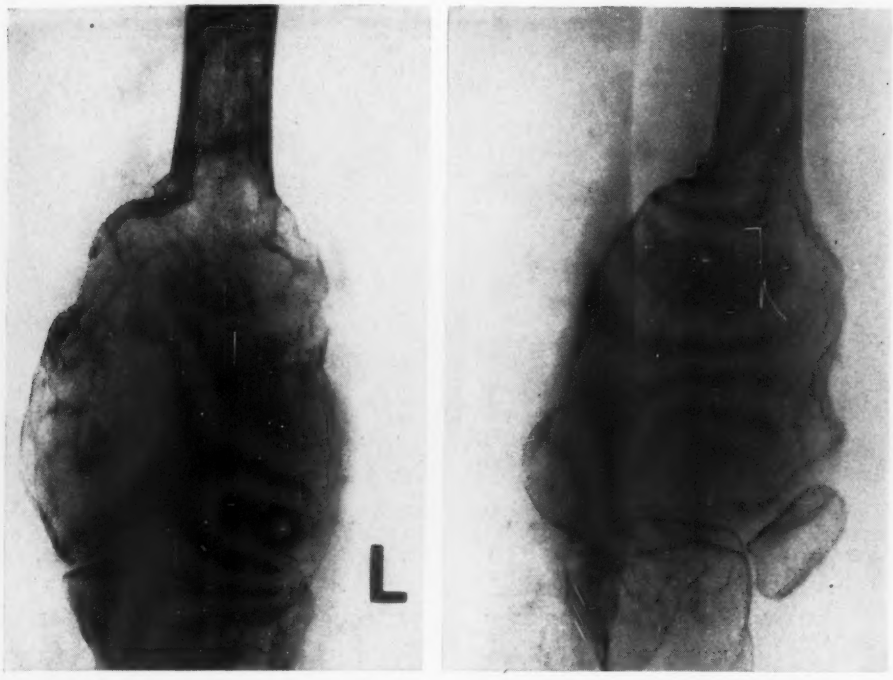


FIG. 4.—(Case 2): Roentgenographic appearance of tumor area four months after institution of roentgen radiation therapy. Observe definite increase in calcification and presence of a definitive cortex surrounding the tumor mass.

able for any major surgery as, while he stated his age to be 58, physiologically, he was a good ten years older and revealed evidence of a relatively marked generalized arteriosclerosis.

Figure 9 exhibits the condition seen on admission. Note the large tumor mass projecting into the popliteal space, which was the basis for the acute symptoms, causing pressure on the posterior tibial vessels and nerves. Roentgenograms of the lungs were negative.

He was, therefore, placed on initial preoperative roentgen ray treatment. On October 5, 1943, the first-stage procedure was carried out. (The operation was initially planned in two stages because of the general poor condition of the patient.) At that time the tumor mass was approached from the posterior aspect, removed, and the tumor within the upper end of the tibia cleaned out. The tumor extended down to the middle third of the lower leg, much farther than was evident in the roentgenograms. Pathologic section confirmed the diagnosis of benign giant cell tumor. By utilization of a plaster encasement it was possible to almost entirely correct the flexion deformity. The wound healed by first intention, but because of the unsatisfactory general condition, it was then decided

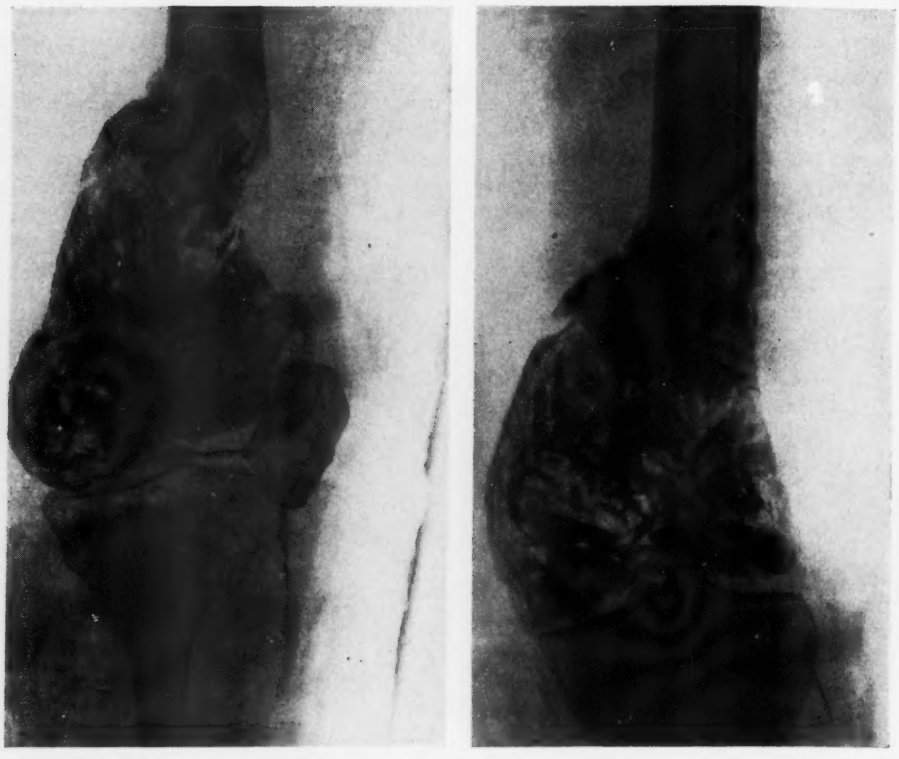


FIG. 5.—(Case 2) : Roentgenographic appearance of the tumor area four months after operation. Multiple bone grafts are beginning to coalesce. There is some deformity of the contour of this part of the bone, but the articular cartilage, though still irregular, has been preserved.

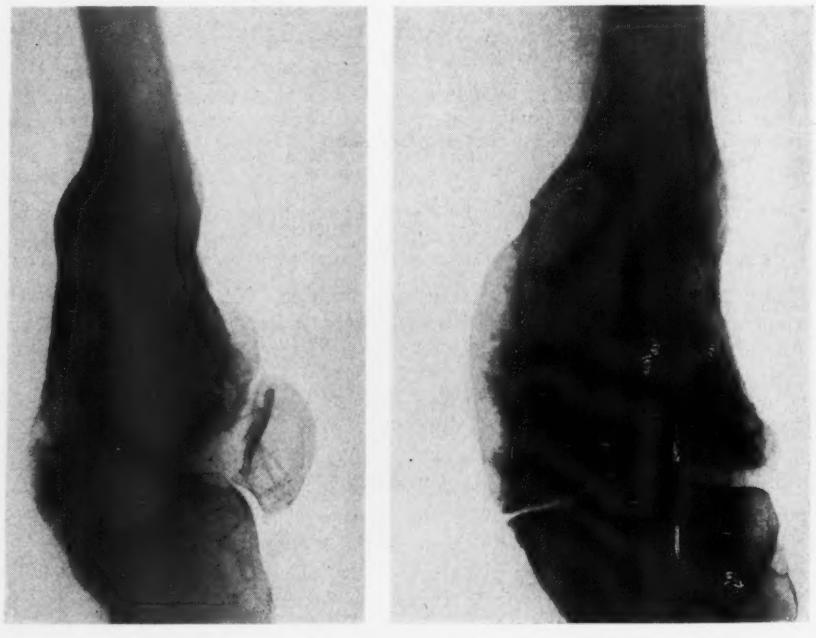


FIG. 6.—(Case 2) : Anteroposterior and lateral roentgenograms eight years following institution of treatment. There is no evidence of recurrence of tumor. Femoral condyles are relatively square and cause limitation of motion in the knee. Patient is exceedingly active and carries on a normal life.

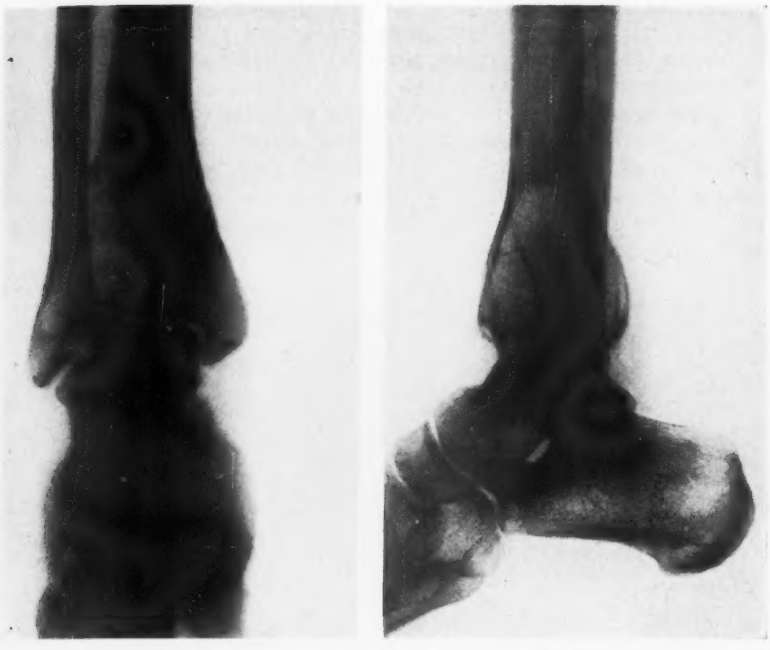


FIG. 7.—(Case 3) : Roentgenograms exhibiting benign giant cell tumor involving the distal end and lateral aspect of the tibia.

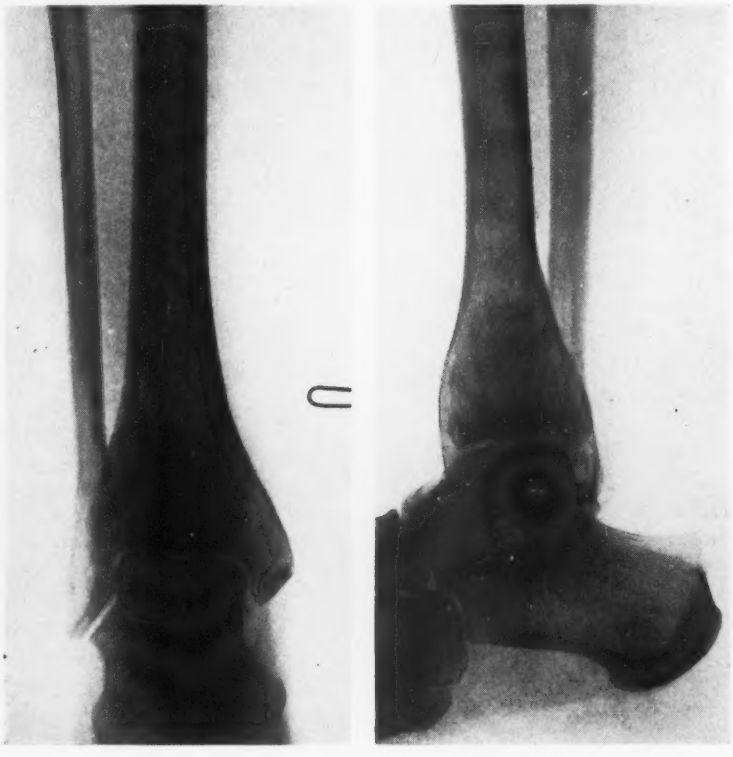


FIG. 8.—(Case 3) : Postoperative anteroposterior and lateral roentgenograms five years after operation. Asymptomatic. Clinical examination including that of the skin is negative. No evidence of recurrence of tumor.

further surgery was contraindicated. Instead of packing the cavity with bone grafts, further roentgen radiation therapy was planned (this is the only patient on whom this program of treatment was followed).

The patient received 1,300 r to each of two ports (anteroposteriorly and postero-anteriorly) preoperatively and 600 r postoperatively to each of two ports laterally. The last examination was on September 17, 1945, at which time there was a 10-degree instead of a 70-degree flexion deformity of the knee, but there was full flexion from this position. He walked without pain or discomfort. The roentgenogram (Fig. 10) did not reveal evidence of recurrence of the tumor.

FIG. 9.—Case 4) : Roentgenogram exhibiting extensive involvement of the upper end of the tibia by benign giant cell tumor. Note large mass projecting into the popliteal space. Pronounced disability.

Case 5.—This 20-year-old housemaid was admitted to the Clinic, February 21, 1944, with the complaint of pain and disability of the left knee region. A pathologic fracture of the lateral femoral condyle occurred on May 22, 1943. A biopsy performed elsewhere revealed a benign giant cell tumor of bone. She was again operated upon on July 17, 1943, elsewhere, and the tumor curetted and bone chips inserted. There was apparently satisfactory progress until February 7, 1944, when roentgenograms revealed a marked increase in cystic changes in the bone and it was thought a malignant tumor was present; amputation was advised.

On clinical examination, the patient revealed an almost complete loss of function in the knee due to pain, with a very marked flexion contracture. The roentgenogram (Fig. 11) in our opinion indicated that it was still a benign giant cell tumor. This was later confirmed when Dr. Shields Warren examined slides of tissue removed at the previous operation.

Preoperative roentgenotherapy was directed through three skin portals, two lateral 10 cm. each and one anteroposterior 15 cm. A total of 1,500 r measured in air was

delivered to each skin area in divided doses, to give a total of 4,500 r, giving a daily dose of 150 r to each portal so as not to produce skin damage. In Figure 12 note the marked increase in bony trabeculation and calcium deposit in the five months following roentgen radiation.

On October 9, 1944, the tumor area was exposed, carefully curetted, no cauterization, and packed with bone grafts. Pathologic report revealed "benign giant cell tumor with unusual osteoid activity, probably due to preceding trauma." It was not considered to be malignant. The patient convalesced uneventfully following this procedure, and was discharged home, October 20, 1944, in a plaster encasement to protect the extremity, walking with crutches.

The last observation was on January 15, 1946, when the roentgenogram (Fig. 13) revealed progressive calcification of the involved area. The external contour of the operative site remains smooth. At this time she was walking without crutches and had no pain or swelling of the knee, and there was no clinical evidence of recurrence. Unable to move the knee on admission she now has 80-degree flexion from full extension. With continued exercises, a further increase in motion is anticipated. Roentgenograms of the lungs remain negative. The skin of the radiated area is of normal appearance.

Case 6.—An 8-year-old girl was admitted to the Clinic, December 11, 1944, because of a persistent swelling of the left hand which had been first noted in August, 1944, and since that time had progressively increased in size to the point where when first seen there was marked loss of function of the hand. Examination revealed a diffuse, pronounced swelling of the region of the fourth metacarpal of the right hand and the roentgenograms (Fig. 14) were characteristic of a giant cell tumor which on the basis of the history was rapidly increasing in size. Inasmuch as all the findings indicated a benign process, she was, therefore, started on preoperative roentgen ray therapy, receiving a total of 600 r through a shielded port so as not to affect the epiphyses.

February 27, 1945, the tumor was exposed by a dorsal incision, cleaned out carefully, no cauterization, and packed with bone grafts. No attempt was made to crush in the walls of the cavity, desirable from a cosmetic point of view, because of the inevitable subsequent disturbance to the metacarpal phalangeal articulation. Pathologic report was benign giant cell tumor, with radiation reaction.

The wound healed by first intention. The patient was thereafter observed at intervals, the last time on January 26, 1946, when she showed normal motion of the wrist and fingers. The swelling had almost entirely disappeared and the skin of the radiated area revealed no change. Roentgenograms (Fig. 15) exhibit a healed lesion and no further evidence of disturbed epiphyseal growth.

Case 7.—A 45-year-old housewife was admitted to the Orthopedic Service, August 15, 1944, with the complaint of pain in the left knee of three months' duration. The pain was so severe she could walk only with crutches and even then with great difficulty. The roentgenograms (Fig. 16) suggested a malignant lesion, as did the history, but at biopsy, August 23, 1944, a definite diagnosis was made of benign giant cell tumor of bone.

Thereafter she received radiation therapy, 1,500 r to each lateral port, for a total of 3,000 r. On December 21, 1944, she was operated upon in the manner described. The pathologic report of the tissue removed revealed benign giant cell tumor with extensive fibrosis due to radiation reaction. The wound healed by first intention and she was discharged home in a plaster encasement, walking with crutches, but returned seven weeks later because she was experiencing some thigh discomfort. Inspection of the site of the wound revealed a definite cellulitis for which she was immediately hospitalized, and within three days developed a small sinus from which serous-like material discharged. It was cultured but no growth obtained. Gradually this reaction subsided and she was again discharged home. The symptoms recurred and she finally was again readmitted and, June 2, 1945, the entire area of the tumor including transplanted bone was cleaned

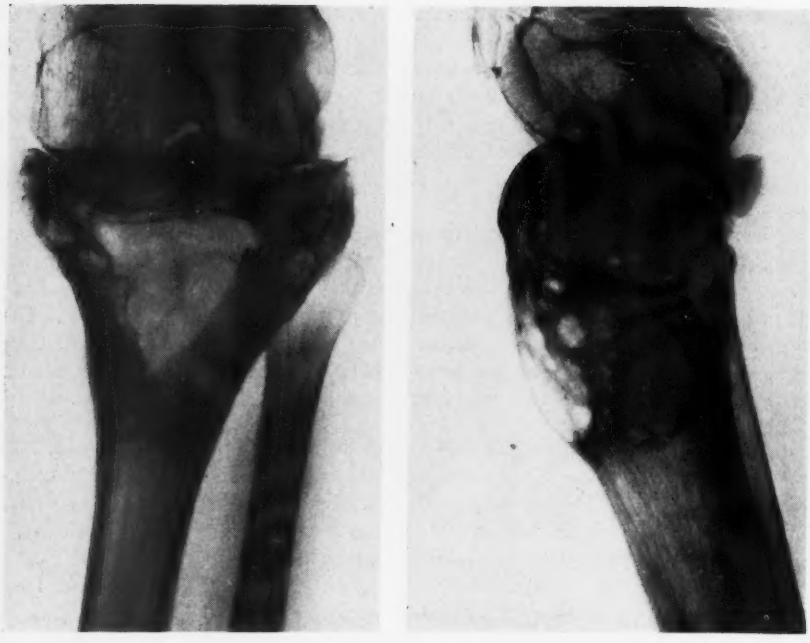


FIG. 10.—(Case 4) : Appearance two years and four months following first-stage operation. Because of poor physical condition an attempt at bone graft was not carried out. Asymptomatic except for a 10-degree persistent flexion contracture of knee joint. Excellent function.

FIG. 11.—(Case 5) : Admission roentgenogram revealing an osteolytic benign giant cell tumor of the lower end of the femur. Observe large mass in the lateral view in the posterior aspect of the femur.

out and much of the wall of the cavity cut away (Fig. 17). A periosteal flap was turned in over the defect. The pathologic report of the material removed at this operation was fibrosis with foreign body reaction. There was no definite evidence of tumor.

Since the above procedure the wound has remained healed and in the last roentgenograms (Fig. 17), February 21, 1946, there is no evidence of tumor recurrence nor of osteomyelitis.

Because of persistent pain affecting the entire extremity, it was believed the patient

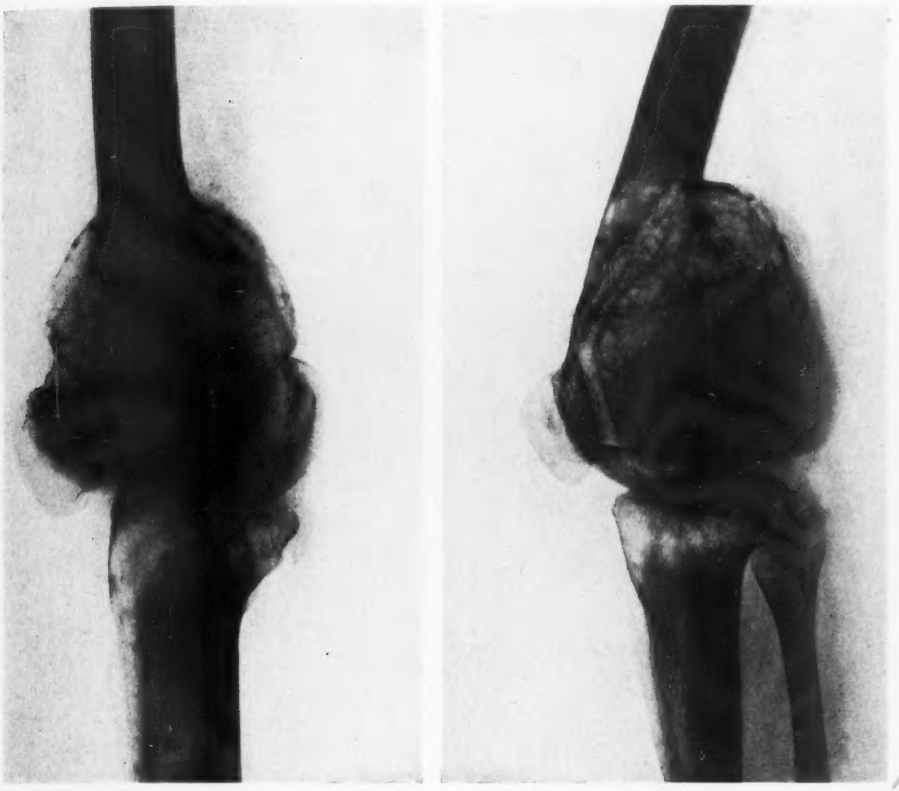


FIG. 12.—(Case 5): Roentgenograms seven months following institution of roentgen radiation therapy. Marked increase in calcification and formation of a definite cortex about the tumor mass.

might also have a true sympathetic dystrophy. This was confirmed by procaine block of the lumbar sympathetic chain and finally a left lumbar sympathectomy was performed by the general surgical service on August 8, 1945, since which time she has been comparatively asymptomatic and is progressively increasing the range of motion in the knee. Patient continues to protect the extremity by walking with crutches, due to the extensive removal of bone. There is no evidence of skin radiation reaction.

RESULTS

Seven patient have received combined roentgen ray and surgical treatment for proven benign giant cell tumor of bone. All are living and well, and over an average period of 4.7 years, exhibit no evidence of recurrence. The longest follow-up is nine years eight months, the shortest one year.

One patient (Case 4) received postoperative radiation treatment because it was not possible to complete the surgical procedure due to the patient's poor physical condition.

All of the operative wounds healed by first intention. In one patient (Case 7), seven weeks after operation, what originally appeared to be a mild cellulitis developed about the site of the previously healed incision. A serous-like dis-

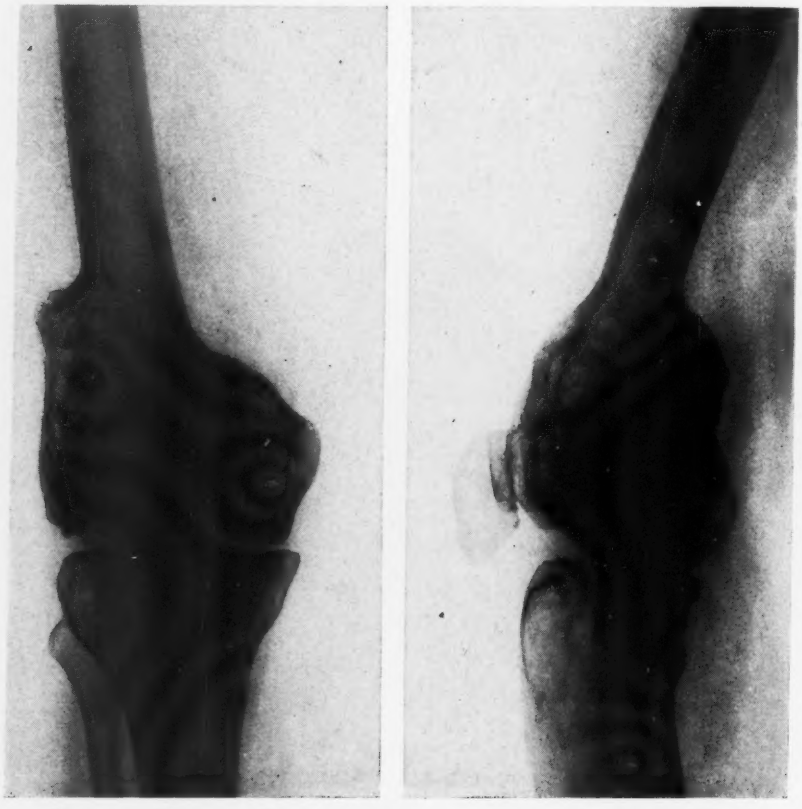


FIG. 13.—(Case 5) : Roentgenograms one year and ten months following institution of roentgen ray treatment and one year and three months following operation. No evidence of recurrence of tumor. The irregularity of the lateral femoral condyle persists. Progressively increasing function of knee joint. Skin over this area negative for any changes.

charge then appeared which on culture revealed "gram-positive cocci in clumps which would not grow out on subculture." Some further attempts to culture this discharge revealed no growth. Under conservative management, the wound healed, the patient returned home, but later it again broke down, necessitating a secondary operative procedure. This wound also healed by first intention and has remained healed for nine months, the patient meanwhile ambulatory. At no time in this patient was there evidence of an osteomyelitis.

The function of the joint adjacent to the tumor has been preserved in all

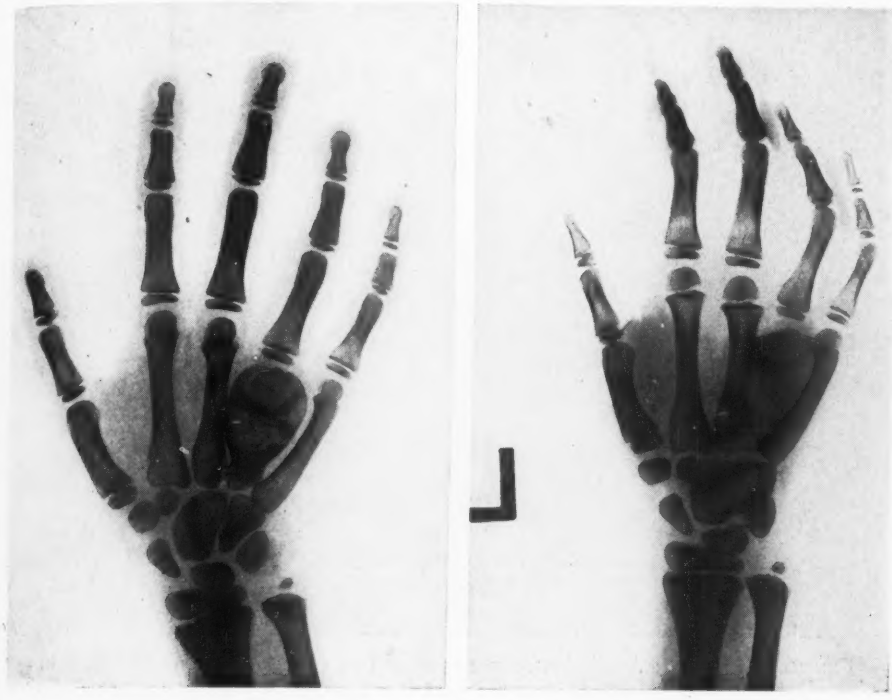


FIG. 14.—(Case 6): Preoperative roentgenograms of a rapidly growing benign giant cell tumor with shortening of metacarpal in a child eight years old.

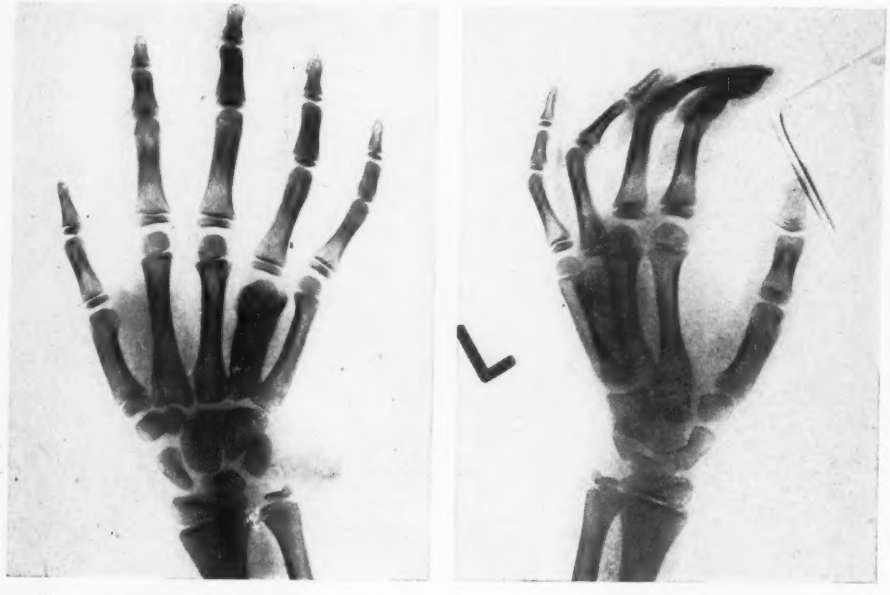


FIG. 15.—(Case 6): One year after operation. On clinical examination the swelling is not apparent. Normal function of fingers and wrist. No evidence of recurrence. Skin negative.

FIG. 16.—(Case 7): Admission roentgenogram of an osteolytic, completely disabling benign giant cell tumor of the lower end of the femur, which suggested malignancy; this disproved by biopsy.

FIG. 17.—(Case 7): Roentgenogram 17 months after institution of treatment following a supplementary procedure that necessitated removing previously placed bone grafts. Wound healed *per primam*. Progressively increasing function of knee joint, now one-half normal. No symptoms and no evidence of recurrence.

patients who on admission revealed a normal appearing articular surface in the roentgenogram. In one patient (Case 6) there appeared to be marked distortion of the anatomy of a metacarpal phalangeal joint. But one year later the fingers and wrist exhibit normal function.

In Case 2 there was definite skin change noted on admission. This was caused by previous roentgenotherapy which in our opinion was given without adequate filtration and as a result of using large skin portals. Roentgen radiation following admission through several small ports did not produce further skin damage.

COMMENT.—Following a review of a large series of cases collected by the Registry of Bone Sarcoma, Codman, in 1937, stressed the fact that a study of these cases indicates the essentially benign nature of the tumor. He concluded that expansion and progress of the tumors are due to their pulsation and not to the malignant quality of their cells. Codman postulated that the structure of a giant cell tumor was analogous to that of a sponge in that there are no walled blood vessels and the corpuscles circulate through the interstices of the tumor as if it were a sponge; hence, this whole sponge pulsates and tends to expand in bony walls by destroying the rigid boundaries. He, therefore, concludes, "it is very important to pay scrupulous attention to stopping the blood supply of the tumors."

On the basis of our experience in operating upon these tumors with and without preoperative roentgen radiation there is no question but that the character of the tumor tissue following roentgenotherapy is very much less vascular when radiation treatment is administered. Also, the histology of the tumor following radiation reveals a marked fibrosis, with pronounced reduction in the cellular character of the tumor.

As a further aid in controlling the blood supply of the tumor area we now plan at operation to utilize the various forms of blood fractions which have become available to check hemorrhage.

It is to be emphasized that the radiation therapy given before surgery in the manner as outlined, did not interfere with wound healing. In one patient (Case 7) it might be argued that the roentgen ray treatment was responsible for the cellulitis that appeared seven weeks after operation. It was true that at the time we were not able to culture an organism. On the other hand, the whole process was an inflammatory one in every way compatible with an attenuated infection or aseptic necrosis. When finally reoperated upon, the wound healed promptly and has remained healed.

It is pertinent to note that no malignant changes have developed in these patients or in any other benign bone lesions which we have subjected to radiation treatment.

We also believe it is extremely important that the involved extremity, with appropriate splintage, be subjected to as near normal use as soon as possible. This program stimulates bone repair, and with the institution of intensive active muscle exercises, hastens recovery.

SUMMARY AND CONCLUSIONS

Seven patients with benign giant cell tumors of bone have been treated by combined roentgen ray and surgical management. In each instance not only has the extremity been saved and there has been no evidence of recurrence of the tumor but the affected extremity is a useful member.

Roentgen radiation therapy, as herein described, has not interfered with the reparative processes of the tissues following surgery.

REFERENCES

1 Codman, E. A.: Treatment of Giant Cell Tumors about the Knee: A Study of 153 Cases Collected by the Registry of Bone Sarcoma of the American College of Surgeons. Surg., Gynec. and Obst., **64**, 485–496, February, 1937.

2 Coley, B. L., and Higinbotham, N. L.: Surgical Treatment of Giant Cell Tumor. ANNALS OF SURGERY, **103**, 821–835, May, 1936.

3 Geschickter, C. F., and Copeland, M. M.: Tumors of the Giant Cell Group. Arch. Surg., **21**, 145–156, July, 1930.

4 Hatcher, C. H.: The Development of Sarcoma in Bone Subjected to Roentgen or Radium Irradiation. J. Bone and Joint Surg., **27**, 179–195, April, 1945.

5 Herendeen, R. E.: Results in Roentgen Ray Therapy of Giant-Cell Tumors of Bone. ANNALS OF SURGERY, **93**, 398–411, January, 1931.

6 Inclan, Alberto: The Surgical Treatment of Giant Cell Tumors of Bone. J. Internat. Coll. Surgeons, **3**, 389–399, October, 1940.

7 Johnson, R. W., Jr., and Lyford, John, 3d: Treatment of Benign Giant Cell Tumor in the Lower Third of the Femur by Curettage and "Telescoping" the Fragments of Bone. J. Bone and Joint Surg., **27**, 557, October, 1945.

8 Kolodny, A.: Bone Sarcoma: The Primary Malignant Tumors of Bone and the Giant Cell Tumor. Surg., Gynec. and Obst., **44**, 1–214, April, 1927.

9 Meyerding, H. W.: Treatment of Benign and Giant Cell Tumors by Resection or Excision and Bone Grafting. J. Bone and Joint Surg., **27**, 196–206, April, 1945.

EPITHELIOMA OF THE ANUS*

HAROLD D. HARVEY, M.D.
NEW YORK CITY, N. Y.

EPITHELIOMA OF THE ANUS is a lesion which is not encountered frequently. It occurs usually as a disorderly growth of squamous cells, but the basal cell and mixed varieties also are seen. The tumors are found at or near the mucocutaneous margin, or within the anal canal, or situated principally within the rectum, sometimes having only a slight gross relation to the epithelium below the pectinate line. Similar growths are also found within the large intestine, clearly distinct from the anus.

Perhaps because no one person has had much experience with these tumors, there seems to be no clear understanding among the medical profession of how they should be treated. The literature only adds to the confusion. Papers have appeared in this country reporting 92 cases from the Mayo Clinic, and ten cases from the Lahey Clinic, and there have been reports of cases treated at l'Institut du Radium in Paris, and others from clinics in London and Germany. These reports, however, do not give in detail the circumstances associated with the lesions which they discuss, or a clear impression of the virtues of the various methods of treatment employed. Cattell and Williams, from the Lahey Clinic, recommend an abdomino-perineal resection with inguinal node dissection "in every case of an operable tumor in which cure is possible and feasible." The 20 cases treated at l'Institut du Radium naturally received radiation therapy, and the difference in reported results of the two methods is not striking. Broder's classification has been suggested as a basis for deciding what form of treatment to use, but this recommendation has by no means been widely adopted. It is with the purpose of clarifying the rationale for the choice of one or more of the various possible forms of treatment that this review was undertaken.

The cases reviewed are 37 which were seen at the Presbyterian Hospital from 1918 to 1944, inclusive. A statistical analysis of so few cases, or even of all the cases appearing in the literature, would be valueless. The method of study, instead, has been to analyze carefully these cases in which the treatment, the follow-up result, and many of the circumstances attending the individual lesions are known. Among the 37 cases, the sex incidence was nearly equal. The age incidence by decades was surprising, as over one-fifth of the patients were under 40 years (Table I).

Table II shows how the cases have been classified. There is little to be learned from the first two groups, composed of patients who received no treatment or had no follow-up record and of those to whom frankly palliative therapy was given. The other three groups are further analyzed.

---

* Read before the New York Surgical Society, October 24, 1945.

The cases referred to in this paper which received radiotherapy, received this treatment under the care of Dr. Maurice Lenz, Professor of Clinical Radiology, College of Physicians and Surgeons, Columbia University.

Although it is often from his poor results that the surgeon learns most, not much information can be obtained from the unsuccessful cases in this series. Some of them perhaps should have been classified with the group which received palliative therapy. The two postoperative deaths do not give a fair estimate of the danger of the abdomino-perineal operation, because one of the deaths occurred in a patient greatly emaciated as the result of chronic ulcerative colitis, in whom the epithelioma was only a small incidental lesion,

TABLE I

AGE INCIDENCE

Age	Cases	Age	Cases
20–29	2	60–69	5
30–39	6	70–79	6
40–49	9	80–89	1
50–59	7	Unknown	1

TABLE II

GROUP CLASSIFICATION

No treatment (5), or no follow-up record (1)	6
Palliative treatment only	9
Unsuccessful treatment	9
Recent cases, still alive (under 3 years)	7
Survived 5 years or more	6
Total	37

TABLE III

UNSUCCESSFUL CASES

Abdomino-perineal resection:		4
Postoper. deaths	2	
Nephritis—9 mos.	1	
Persistent tumor	1	
Perineal proctectomy		1
Radiation (one lived 4 years with the disease)		4
Total		9

TABLE IV

RECENT CASES, STILL ALIVE (UNDER THREE YEARS)

Case	Treatment	Size of Tumor
M. G.	Perineal proctectomy plus roentgen ray	½ encircling
C. S.	Radium needles, unsuccessful. Later, abdomino-perineal	⅔ encircling
A. M.	Radium needles, later abdomino-perineal	½ encircling
J. D.	Abdomino-perineal. Later, excision of tumor in inguinal nodes	⅔ encircling
S. A.	Abdomino-perineal	3 x 2 cm.
O. B.	Abdomino-perineal	¾ encircling
R. B.	Radium needles	Nearly encircling

and the other followed an heroic effort to dissect around an extensive tumor, during which the right internal iliac vessels were resected. One patient died of nephritis only nine months after his operation. The other six cases all died of persistent tumor, one committing suicide to end his suffering. One patient lived for more than four years before succumbing. None of the tumors, except the incidental one, was small. Most of them were extensive and could have been given a bad prognosis before treatment was started.

The cases treated within the last three years, and who are still alive, illustrate how the tendency has been to rely more and more upon abdomino-perineal resection. Three were treated by means of radium needles, but in two of these, operation was subsequently performed for persistence of tumor. The third has not yet been followed over two years. With one exception these tumors were fairly extensive, encircling the anus one-half or more. Following one of the abdomino-perineal operations, metastases have appeared in the inguinal nodes, which were not resected at the time of the original operation. In three of the six cases operated upon, metastases in the perirectal nodes were demonstrated. The smallest tumor in the group, three centimeters

FIG. 1.—Tumor in rectal wall.

in diameter, was one that had metastasized. It is not known, of course, whether the nodes in the patient treated by radium needles are involved.

All of these patients required vigorous methods of treatment because of the extent of the lesions. In none could local excision have been logically considered as a means of cure. In the cases which proved to have involvement of the perirectal nodes, nothing but a radical operation could be expected to be successful because radiotherapy can not be relied on to eradicate tumor in the nodes. We do not know the final results of treatment, but we can show that radiation, as it was applied, had to be followed by radical surgical excision in two cases, and that an abdomino-perineal operation was followed by excision of involved inguinal nodes which had not been removed at the original operation.

One patient seems to demonstrate a point in the technic of radiotherapy.

Case 1.—Chart No. 706628: C. S., a male, age 37, had symptoms for one month, consisting of a constant desire to defecate and blood in the stools. He had a mass which distally involved the pectinate line, extended up the rectal wall for over two centimeters, and which occupied over half the circumference of the anorectal region posteriorly. Biopsy revealed squamous cell epithelioma. No inguinal nodes were found that were suspected of involvement. His general health was excellent.

He was treated interstitially with 11 radium needles, 6 cm. long, giving a total of 9,000 mg. hours. The tumor disappeared, but eight months after treatment it reappeared, extending up the rectal wall for six centimeters. An abdomino-perineal resection was then performed, with removal at the same time of some enlarged inguinal nodes. No metastases were found in these or in the pelvic nodes. It is a year from operation and the patient so far is apparently well.

A photomicrograph shows the persistent tumor as it was when removed at operation, lying in the rectal wall (Fig. 1). A section taken distal to this, in the region where the tumor presumably originally lay, shows only scar tissue where the radium needles had been placed, but no evidence of tumor (Fig. 2).

This case suggests the necessity for extending the effective field of radiation well up above the gross limits of the tumor, for the recurrent tumor in this case lay principally above the radiated field.

TABLE V

CASES SURVIVING FIVE YEARS OR MORE

Case		
G. F.	Small tumor. No metastases. Perineal proctectomy	Died 5 years, without tumor
M. D.	Tumor arose after radiation for pruritus	Died 12 years of tumor
A. R.	Perineal proctectomy. Growth encircled ½ anus. Four perirectal nodes had metastases	Alive 9 years plus
A. H.	Small tumor. Local excision followed by radium pack	Alive 8 years plus
A. R.	Small tumor. Local excision	Alive 7 years plus
P. A.	Growth nearly surrounded anus. Radium needles. 4651 mg. hrs.	Alive 8 years

The six cases included in Table V, out of the 37 who came originally to the hospital, include four who were alive, without evidence of tumor, followed for nine, eight, eight and seven years, one who died of heart disease but without evident tumor five years after treatment, and one who died of tumor after 12 years. The last should perhaps not be included in the series at all because her tumor arose near the anus in an area of skin which had been irradiated for treatment of pruritus. She underwent numerous procedures, none of which successfully checked the spread of the disease.

It is noteworthy that three of the remaining five cases had small tumors, approximately two centimeters in diameter. The fourth had a tumor which half encircled the anus, with metastases to four perirectal nodes. She was successfully treated by a perineal proctectomy. The fifth had a growth that nearly encircled the anus, which was a basal squamous cell type of epithelioma, and which was successfully treated by interstitial radium needles, giving a calculated dosage of 4,651 mg. hours. The method of treatment of the small tumors was simple local excision for one, perineal proctectomy for the second

(no metastases were found) and excision biopsy followed by radium pack for the third.

The last case is of interest in illustrating the factors which can enter into the choice of treatment of this disease.

Case 2.—Chart No. 397947: The patient was a woman, age 32, recently married, and two months pregnant, who complained of intermittent rectal bleeding for two months, and who had a papillary mass, two centimeters in diameter, in the pile-bearing area in the left posterior quadrant. Under caudal anesthesia, "resection of the mass was carried out by means of the high frequency knife. A cuff of apparently normal mucosa was left on

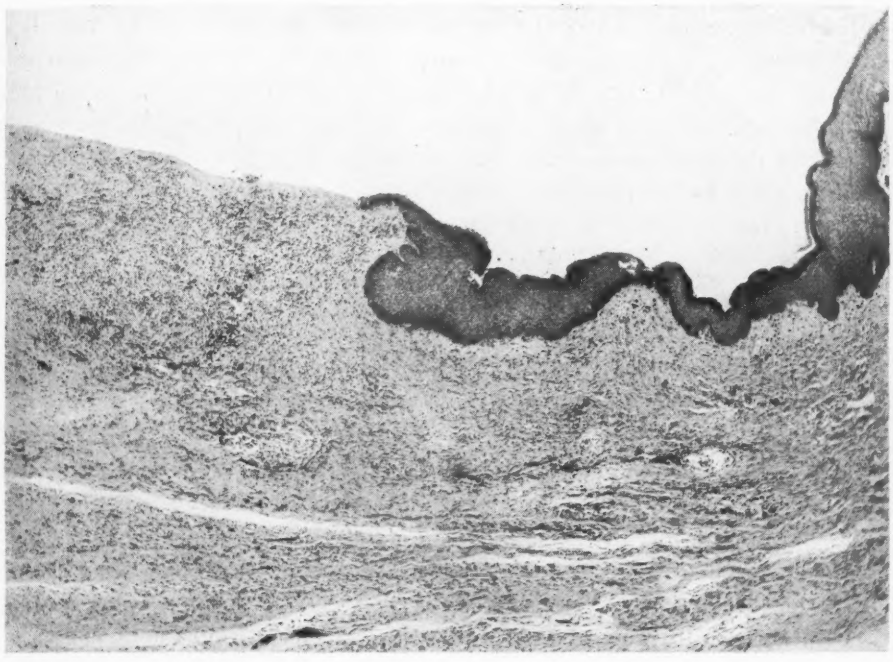


FIG. 2.—Scarring and ulceration, but no tumor where radium needles were inserted.

either side, and some of the underlying muscles were also removed. However, the sphincteric apparatus was in no way damaged to such an extent that incontinence might follow." The mass had previously been biopsied and squamous cell epithelioma reported. The microscopic study of the tissue excised with the high frequency knife showed the following: "The tumor has obliterated the normal architecture of the mucocutaneous junction, and is mostly located superficial to and above the internal sphincter. Superficial portions of the sphincter and the rectal muscularis have been invaded by the growth. The surface is formed of ulcerated, very vascular, thick papillary projections, lined by tumor cells and containing masses of tumor distributed irregularly throughout. . . . Epithelioma cells are found filling one small vessel deep to the main growth."

Largely on the basis of the finding of the tumor cells in the lymphatic vessel, so close to the margin of resection, the patient was advised to have a therapeutic abortion, to be followed by an abdomino-perineal resection. She had the abortion performed, but refused to be operated upon. Instead, she went to Dr. George T. Pack, at the Memorial Hospital, who "inserted a special rectal radium applicator within the anal

canal. This instrument is designed to give surface irradiation to the entire surface of the anal canal and terminal rectum. A filter of three millimeters of brass was employed and a dose of 600 milligram hours administered on each of two successive days." She had discomfort from proctitis for almost a year, but has retained full function of the bowel, has since had a child, has been free of symptoms for seven years and has no evidence of tumor, now, eight years since treatment. What part the radium played in her recovery one cannot say.

This last group of cases, five of whom appear to have been successfully treated, are the most interesting of the series. They illustrate most of all that each patient with epithelioma of the anus should be considered as a distinctly individual problem. No one form of treatment is applicable to all. The small tumor may perhaps be justifiably treated very differently from the large tumor. If the patient is intelligent enough to understand in general the risks and *sequelae* of the various forms of treatment open to him, his wishes should be the controlling factor in their choice. In retrospect, it would have been an error to have subjected patients A. H., A. R. and P. A. to radical surgery. None of the three small tumors that we encountered had metastases.

CONCLUSIONS

1. The majority of cases of epithelioma of the anus come to the doctor too late for arrest of their disease by any known treatment.

2. For large growths, or growths with metastases, a radical resection of anus and rectum with removal of the inguinal nodes should offer the best chance of arrest. The indication for a procedure of this kind is clearest in the tumors which are neither extensive nor small, for in the former the prognosis is bad with any therapy and in the latter less mutilating measures may succeed. The perineal dissection, if undertaken, should be wide, as extension of the tumor into perirectal structures is common.

3. Radiation therapy may control growths which are locally quite extensive, but cannot be counted upon to destroy tumor deep in perirectal nodes. Metastases of this kind are frequent in tumors that involve half or more of the anus. If successful, radiotherapy has obvious advantages over treatment by radical operation. If employed, it should include in the effectively radiated field a portion of the rectal wall well above the gross upper limits of the tumor. The discomfort following radiation may for some months be extreme. Radiotherapy should usually be preceded by a temporary colostomy.

4. For small tumors, two centimeters in diameter or less, radical operative therapy, while perhaps the safest from standpoint of saving life, may be justifiably avoided. Arrest may follow local removal, radiotherapy, or a combination of the two.

5. In order that early diagnoses may not be missed, the medical profession should be aware that these tumors are found with relative frequency in people under age 40, and occur especially in relation to fistula in ano and other sources of chronic irritation about the anus.

REFERENCES

1 Kerr, J. G.: Squamous Cell Carcinoma of the Anorectal Region. Texas State J. of Med., **36**, 548, 1940.

2 Cattell, R. B., and Williams, A. C.: Epidermoid Carcinoma of the Anus and the Rectum. Arch. Surg., **46**, 336, 1943.

3 Keyes, E. L.: Squamous Cell Carcinoma of the Lower Rectum and Anus. ANNALS OF SURGERY, **106**, 1046, 1937.

4 Gabriel, W. B.: Squamous Cell Carcinoma of the Anus and Anal Canal: An Analysis of 55 Cases. Proc. Roy. Soc. Med., **34**, 139, 1941.

5 Niedermayr, R.: Die kombinierte Radium-Rontgenbehandlung der Rektum und Analkarzinome. Strahlentherapie, **58**, 624, 1937.

6 Bensaude, Cain, Oury, et Poirier: Le Cancer de l'Anus. Presse Med., **41**, 1837, 1933.

CUSHING'S SYNDROME*

PETER HEINBECKER, M.D.

ST. LOUIS, MO.

FROM THE DEPARTMENT OF SURGERY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, AND BARNES HOSPITAL, SAINT LOUIS, MO.

IT SEEMS FITTING to discuss Cushing's syndrome in a symposium honoring the work of Dr. Allen O. Whipple, whose scholarly and inquiring spirit has placed him along with Cushing in that elect group of men whose work has made the accomplishments of American surgeons noteworthy among men of science.

After 20 years of observation, Cushing (1932) published an analysis of a group of cases exhibiting a pluriglandular syndrome which since then has often been referred to as Cushing's syndrome. While many no longer accept his concept of its pathogenesis, his description of the clinical state and his analysis of the relevant glandular interrelationship have served to establish it as a clinical entity and to extend our knowledge of endocrinology immeasurably.

THE SYNDROME

The essential characteristics of the syndrome are, in brief: (a) painful adiposity confined to the face, neck and trunk; (b) kyphosis of the upper thoracic spine; (c) hypertrichosis of the face, neck and trunk in females and preadolescence in males; (d) dusky plethoric appearance of the skin with purplish *lineae atrophicae* on the abdomen and thighs; (e) hypertension; (f) variable backaches, abdominal pains and ultimately extreme weakness; and (g) dryness of the skin with acne and susceptibility to skin infections. Other features frequently but less consistently present were hyperglycemia, glycosuria, diminished sugar tolerance, polyphagia, polydypsia, osteoporosis, bronze pigmentation of the skin, *cutis marmorata* and purpuric ecchymoses.

Of the 12 cases reported on by Cushing, three had a small but definite basophil adenoma, two an undifferentiated adenoma and one a questionable adenoma of the hypophysis. Two had pituitary glands with normal gross appearance. Although aware of the fact that, clinically, similar syndromes had been found associated with tumors of other endocrine glands, particularly the adrenals, Cushing, nevertheless, hypothesized that the primary cause of the disturbance was a basophil adenoma of the hypophysis.

PRIMARY CAUSES OF CUSHING'S SYNDROME

The problem of determining the primary cause of the syndrome has been beset with difficulty because no single initiating condition has been found. Cushing's original belief that a basophil adenoma was responsible is regarded as erroneous because it since has been shown that basophil adenomas are

* Supported by a grant in aid of research by the Commonwealth Fund.

found unassociated with the syndrome and the syndrome is found without an associated basophil adenoma. Moreover, the cells of a basophil adenoma are nongranular and presumably nonsecretory. It has been shown that basophil cells are trophic to the thyroid and to the germ cells, both of which characteristically are depressed in their function in Cushing's syndrome (Heinbecker, 1944).

As more and more cases have been studied, it has become apparent that in persons exhibiting the syndrome, the primary cause may be (1) an adrenal cortical tumor; (2) a tumor of the ovary; or (3) a tumor of the thymus. In a group of cases without any primary tumor, it has been shown (4) that the initiating cause may be an atrophy of the paraventricular nuclei of the hypothalamus and to a lesser degree an associated atrophy of other hypothalamic nuclei, including the supra-optic and the mamillary (Heinbecker, 1944). Case 1 is cited as an example (Fig. 1).

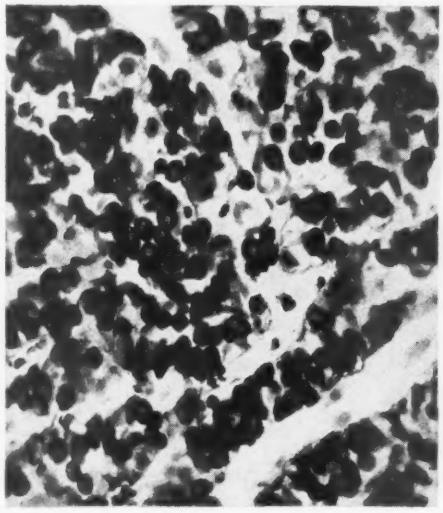


FIG. 1.—Photomicrograph (x 680) from anterior lobe of the hypophysis of a "puncture" dog showing eosinophils and chromophobes with no basophils remaining.

Crooke (1935) described a degranulation or hyalinization of the basophil cells of the hypophysis in persons exhibiting Cushing's syndrome. This finding, confirmed by others, including Rasmussen (1936), may be regarded as present in all true examples of the syndrome. The problem of pathogenesis resolves itself into determining how the various primary causes above listed may lead to degranulation or hyalinization of the basophil cells of the hypophysis.

EXPERIMENTAL AND CLINICAL INVESTIGATIONS

Heinbecker (1944) reported that in "puncture" dogs in which the neural hypophysis was denervated through the oral approach by a puncture wound separating it from the supra-optic and paraventricular nuclei, there occurred a loss of basophil cells in the glandular hypophysis (Fig. 2). The eosinophil cells thereby became dominant. Such a change is complete within a year. The actual time-interval necessary for complete disappearance of the basophil cells has not been determined. Partial granulation may still be present in cells three months after making the lesion. By comparing the histology of the other endocrine glands of a dog without basophil cells with those in a totally hypophysectomized dog, it is possible to determine the target organs of the eosinophil and the basophil cells. Such studies have shown that the eosinophil cells are trophic to the adrenal gland, to the prostate, to the inter-

stitial cells of the testis and to the corpus luteum. The basophil cells are trophic to the thyroid gland, to the ovarian follicle and they are essential for the maturation of the germ cells.

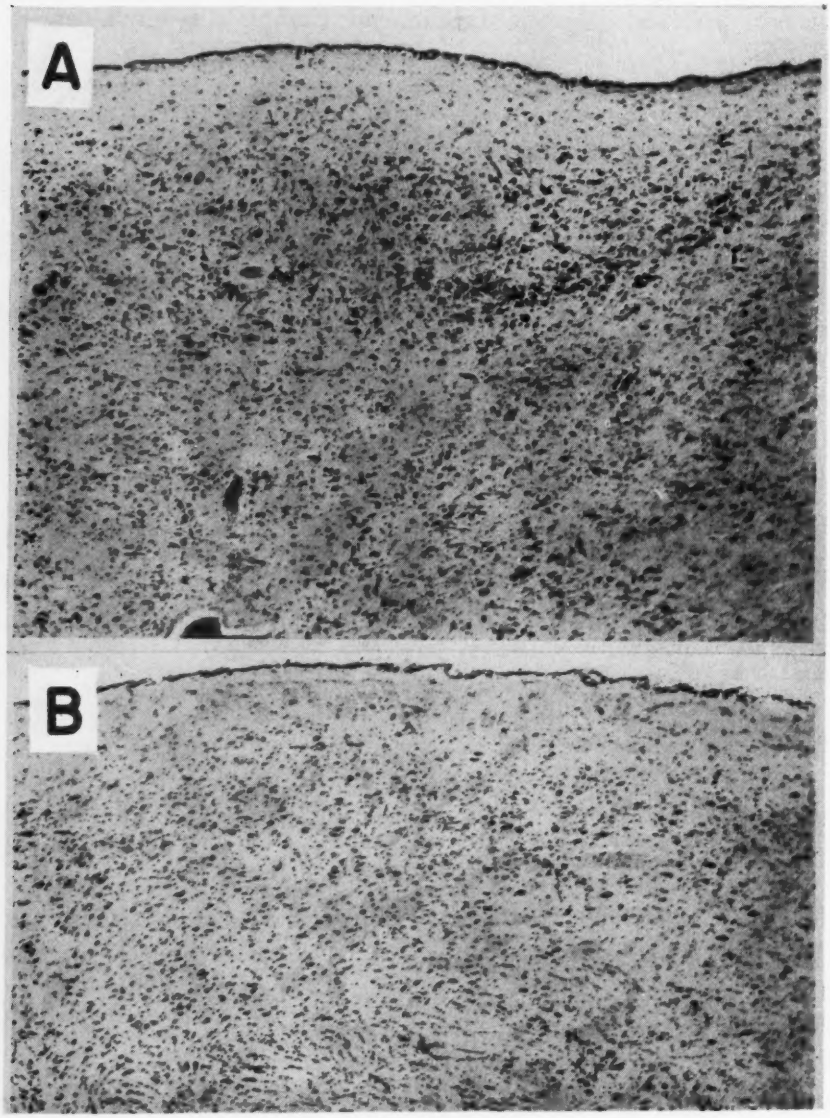


FIG. 2.—(A) Photomicrograph of paraventricular nucleus (x 45) of normal brain, female, age 40.
(B) Paraventricular nucleus (x 45) from Case 1. Note marked loss of cells as compared with the normal.

In other experiments in the dog, lesions were made caudal to the stalk to interrupt fibers coming from or going to the paired paraventricular nuclei. In such dogs it was found that no retrograde degeneration occurred in the

cells of the paraventricular nuclei but the animals nevertheless became obese and lost most of the basophil cells in the glandular hypophysis. Those cells which remained have few granules. The inference is drawn that fibers reaching the paraventricular nucleus from more caudal parts of the nervous system are afferent and excitatory. Their interruption results in a depression of function of the paraventricular nucleus.

In man exhibiting Cushing's syndrome, degranulation of the basophil cells is not complete; it is only partial, and has been described by some as an hyalinization. In the "puncture" dog the change in the cytology of the glandular hypophysis is more pronounced and is attributed to a more marked depression of the secretion of the neural hypophysis, or it may be a species difference. It seems logical that if it could be shown that the hormones of the tumors, which have been regarded as primary causes of Cushing's syndrome, result in a depression of the action of the neural hypophysis by neutralization of its secretion, a similar cytologic change in the glandular hypophysis should be effected.

Adequate evidence is available to establish that desoxycorticosterone is an antagonist of the hormone of the neural hypophysis. When given to dogs in fairly large dosage, a state indistinguishable from *diabetes insipidus* results (Ragan, *et al.*, 1940; Mulinos, *et al.*, 1941). It appears reasonable to assume that hormonally active tumors of the adrenal cortex causing the signs and symptoms of Cushing's syndrome secrete sufficient desoxycorticosterone or desoxycorticosterone-like substance to neutralize the secretion of the neural hypophysis, whereby degranulation or hyalinization of the basophils would be effected. In fact, evidence of a rise in serum sodium and a depression of serum phosphorus has been reported (McQuarrie, *et al.*, 1937) and offers supporting evidence for the above assumption. Such depression of the basophil cells would be associated with a dominance of the eosinophil cells, actual or relative (Heinbecker, 1944, *loc. cit.*). Recently Mellgren (1945) has made counts of the cells of the hypophysis in a case of Cushing's syndrome due to an adrenal tumor. He demonstrated an increase in the eosinophil cell count over the average normal control count.

The similarity of chemical structure of desoxycorticosterone and progesterone is established. Likewise, it has been shown that in the pregnant albino rat, the survival time after adrenalectomy was prolonged during pregnancy in spite of the fact that in every case abortion or resorption of the foetuses occurred (McKeown and Spurrell, 1940). The life-maintaining effect of crystalline progesterone has been demonstrated in adrenalectomized ferrets by Gaunt and Hays (1938). The ability of progesterone to neutralize, *in vitro*, the action of posterior pituitary extract on the estrogen primed uterine muscle has been demonstrated by Reynolds and Allen (1935). On the basis of such evidence one might expect a tumor of the ovary with the capacity to secrete progesterone or progesterone-like substances to bring about hyalinization of the basophil cells of the glandular hypophysis by neutralizing the effect of the hormone of the neural hypophysis. Such a case with the clinical and pathologic

findings characteristic of Cushing's syndrome, including polyuria and hyalinization of the basophil cells, has been reported by Norris (1938). In this instance a tumor of the ovary was proven to be the primary cause. It was not established by actual test that the secretion of the tumor was progesterone. However, it is known that large amounts of estrogenic substances do depress the eosinophil cells and do not bring about a depression of the hypophysial basophil cells (Zondek, 1941). It also has been observed in this clinic that a large tumor of the adrenal cortex, bringing about only marked androgenic effects, did not cause any of the signs and symptoms characteristic of Cushing's syndrome (Case 2). It is assumed, therefore, that the changes in the hypophysis characteristic of Cushing's syndrome are not produced by the androgens. By a process of exclusion it is assumed that the hormone secreted by the tumor in the case reported by Norris must have been progesterone or a progesterone-like substance, and that when secreted in large amounts this substance can neutralize the secretion of the neural hypophysis.

The other primary cause of Cushing's syndrome, a tumor of the thymus, presents in the present state of our knowledge greater difficulties of proof. No evidence as to the nature of the hormone of such a tumor is available. Analysis of the clinical record of two such cases (Leyton, Turnbull and Bratton, 1931) shows, however, that polyuria was present in both and Crooke demonstrated hyalinization of the basophil cells in each (1935, *loc. cit.*). Because of the existence of polyuria it seems reasonable to assume that the hormone of the thymic tumor itself or indirectly through overaction of the adrenal cortex was one capable of causing neutralization of the hormone of the neural hypophysis. Obesity was observed also, indicating an overbalanced function of the adrenals, to which the eosinophil cells of the hypophysis are trophic. In both instances definite hypertrophy of the adrenals was demonstrated at autopsy.

The above experimental and clinical evidence, while not complete, is regarded as adequate to support strongly the concept of the pathogenesis of Cushing's syndrome submitted. It would seem to harmonize heretofore conflicting data. It is suggested that either because of a decrease of the secretion of the neural hypophysis, because of hypofunction of the hypothalamic nuclei which control its secretion, or through excess secretion of a neutralizing hormone from a tumor of the adrenal cortex, of the overy, or of the thymus, a change in the cytology of the glandular hypophysis is effected which results in a dominance of the eosinophil-adrenal cortical hormone complex over the basophil-thyroid hormone complex. Changes in other endocrine glands follow as a result of depression of the neural hypophysis and of cellular balance in the glandular hypophysis.

CORRELATION OF EXPERIMENTAL WITH CLINICAL DATA

In those instances of Cushing's syndrome where the primary lesion is an atrophy of the cells of the supra-optic and paraventricular nuclei, the polyuria can be explained with adequate experimental support as the result of a depre-

sion of the secretion of the neural hypophysis secondary to the depression of these nuclei (Heinbecker and White, 1941). When the primary cause is an adrenal cortical, ovarian or thymic tumor the supra-optic and paraventricular nuclei have been found cytologically normal and presumably are then functionally active. Pólyuria then would be the result of a neutralization of the hormone of the neural hypophysis by the hormonally active secretion of the particular tumor concerned. The experimental evidence to support this interpretation is favorable but incomplete where a thymus or ovarian tumor is the primary cause.

The obesity which is always present is regarded as secondary to an increased appetite and also to an alteration in the metabolism of the body whereby fat is formed and stored excessively, a consequence of the overbalanced activity of the adrenal cortical-eosinophil hormone complex, secondary to diminished function of the neural hypophysis. Under such circumstances, marked obesity has been observed in the dog (Heinbecker, White and Rolf, 1944).

The decrease in sugar tolerance which is altered and which may be sufficient to warrant a diagnosis of *diabetes mellitus* may also be attributed in part to the overbalanced action of the eosinophil-adrenal cortical hormone complex. Support for this interpretation has been given by the recent evidence of Price, Cori and Colowick (1945) that anterior pituitary extract inhibits the utilization of glucose by animal tissues, an inhibition which is counteracted by insulin. In the puncture dog lacking the hormone of the neural hypophysis and with eosinophil cell dominance, insulin insensitivity has been demonstrated (Heinbecker and Rolf, unpublished data). It has been shown previously that insulin sensitivity is due to a decrease in eosinophil cell function (Heinbecker and Rolf, 1944). The dog apparently does not react to diabetogenic influences to the same degree as does man. A diabetogenic influence of the adrenal cortical hormone has been established by Long, *et al.* (1940). Clinical experience supports the concept that the development of obesity and of generalized arteriosclerosis tend to precipitate the state of diabetes mellitus.

Persons exhibiting Cushing's syndrome develop diastolic hypertension and arteriolar sclerosis, the mechanism of which is being investigated. Observation in this laboratory on the control of renal blood flow in dogs by a hormone of the eosinophil cells of the glandular hypophysis working in combination with the adrenal cortical hormone (Heinbecker, Rolf and White, unpublished data), together with other observations concerning glandular interrelationships in general has led to the following concept of the pathogenesis of hypertension in Cushing's syndrome, evidence in support of which will be presented in detail elsewhere.

In brief, it is held that the neural hypophysis is activated or inhibited by other portions of the nervous system. A decrease of the secretion of the neural hypophysis results in a dominance of the eosinophil cells and a decrease or degranulation of the basophil cells of the glandular hypophysis. The eosinophil cells are trophic to the adrenal gland, the basophil cells to the thyroid gland. A neutralization of the secretion of the neural hypophysis by desoxycor-

ticosterone, by renin, or by progesterone has a similar effect on the cytology of the glandular hypophysis as does a decrease in the secretion of the neural hypophysis. The action of such a mechanism offers an explanation as to how the glandular hypophysis can be modified by the nervous system *via* the neural hypophysis *without any direct nervous connection.* A depression of the secretion of the neural hypophysis or its neutralization by other hormones results in a sensitization of the blood vessels to epinephrine, to renin, and to the desoxycorticosterone eosinophil complex. Diastolic hypertension results from the action of epinephrine, or renin and of the desoxycorticosterone-eosinophil complex in narrowing extrarenal blood vessels in the sensitized animal. The factors responsible for the functional narrowing of the blood vessels also serve as dominant factors in producing the changes characteristic of arteriolar sclerosis. To them can be added the effect of the hypertension itself and a decrease in the thyroid-basophil hormone complex.

Investigations previously reported showed that in persons with Cushing's syndrome content of calcium salts in the vessel walls becomes markedly increased while the skeleton becomes decalcified. A similar tendency is exhibited in many persons with advancing age and with arteriosclerosis. No definite evidence implicating abnormal function of the parathyroid glands in the altered disturbance of calcium salts has been observed clinically. Experimental evidence that the parathyroids are under the trophic influence of the hypophysis rests on the demonstration by some of a decrease in serum calcium after the administration of anterior lobe hormone. However, the results of other investigations of this subject have been negative. The impression has been gained in this laboratory that under experimental conditions in the dog where there is a marked increase in the basophil cells and a decrease in the eosinophil cells of the hypophysis, the parathyroid glands become enlarged. This would lead to the suspicion that in Cushing's syndrome the function of the parathyroid glands might be decreased rather than increased. At present, the experimental evidence is inadequate to explain the decalcification of the skeleton observed in the syndrome other than that it is associated with the development of the generalized arteriosclerosis.

The changes observed in genital function are readily harmonized with the experimental data. The depression of the basophil cells would lead to a depression of the ovarian follicles in the female and thus to a decrease in menstruation. In the male it would lead to a depression of the maturation of the spermatids. The overaction of the eosinophil-adrenal cortical hormone complex should lead to some increase in the excretion of the ketosteroids in the urine.

Discussion.—The pathogenesis of Cushing's syndrome is outlined in terms of endocrine imbalances precipitated by disturbances of function of the central nervous system or by the excessive secretion of tumors with endocrine function. It is realized that these endocrine imbalances produce in certain individuals signs such as the dusky plethoric moon-face which distinguish the syndrome, and that somewhat similar imbalances do not produce them in other individuals. It seems desirable therefore to postulate that in the indi-

viduals who respond with the true syndrome there exist one or more constitutional factors in the blood vessels and possibly in other tissues which condition their response. Of their nature, nothing yet is known.

SUMMARY

A concept of the pathogenesis of Cushing's syndrome is presented.

Four causes of the syndrome are regarded as being primary, a tumor of the adrenal cortex, a tumor of the ovary, a tumor of the thymus, or an atrophy or inhibition of the hypothalamic nuclei, particularly the paraventricular and the supra-optic.

Experimental evidence is reviewed to indicate how these four primary causes depress the function of the neural hypophysis and effect a dominance of the eosinophil-adrenal cortical hormone complex over the basophil-thyroid hormone complex. Reference is made to the changes which result in other endocrine glands.

The extent to which such alterations in function of the hypophysis explain certain of the clinical signs and symptoms of the syndrome is indicated.

CASE REPORTS

Case 1.—White, married female, age 33; well until five years before admission to Barnes Hospital, when she began to notice increased hair growth on face, blurring of vision and slight ankle edema. During the five years of illness she periodically experienced polyphagia and polyuria. For two years before admission she suffered from ulcers on her legs. Her skin became dry and scaly; she developed stiffness and weakness of her muscles. Frontal headaches and drowsiness were present for two years. For the past year she did not menstruate. During the six months prior to her death her face became full and rounded; her complexion florid. In five years her weight increased from 160 to 208 pounds. Purple striae appeared over the lower abdomen and thighs. Physical examination on admission revealed a patient with an appearance typical of Cushing's syndrome. She had hypertension 200/140; a diminished sugar tolerance; basal metabolic rate −22; daily urine output varied from two to five liters, N.P.N., 35 mg. per cent.

The patient's chief reason for being in the hospital was to have the ulcerations on her legs treated. The ulcers became infected and the infection spread widely beneath the skin and muscles. A streptococcal septicemia finally caused her death.

The essential autopsy findings were: hyalinization of the cytoplasm of the basophil cells of the pituitary; basophilic invasion of the posterior lobe of pituitary; increased pigmentation of the inner zone of the cortex of adrenal; obesity of trunk and face; hirsutism; striae of skin of abdomen and right thigh; unhealed infected amputation wound of left knee; draining wounds of left shoulder (abscess drained 13 days ago); healed wounds of right lower leg (recurrent ulcers); edema of subcutaneous tissue of right lower leg; ecchymosis with superficial bullae of skin of the left flank; edema and congestion of lungs; congestion of liver; focal fatty degeneration of liver; local fatty degeneration of kidneys; hyperplasia of spleen; atrophy of pancreas (45 grams); hyperostosis of bones of skull; focal necrosis with intranuclear inclusion bodies in adrenal and liver; simple cyst of the ovary (10 x 10 x 8 cm.). No pituitary adenoma was present.

Serially cut sections, 20 and eight mm. in thickness, through the pre-optic and hypothalamic regions, stained with cresyl violet, revealed marked loss and atrophy of the nerve cells in the various nuclei of this region. These changes were particularly striking in the supra-optic and the paraventricular nuclei. The ependymal lining cells of the third

ventricle showed a similar atrophy. Round cell infiltration was lacking. While the blood vessels showed intimal thickening and vacuolization of the endothelial lining cells, such changes were not specific for these regions. Sections were taken at random from the thalamus and brain-stem, and even when they showed vessel changes showed no nuclear atrophy similar to that seen in the hypothalamus.

Case 2.—Colored female, age 19, entered Barnes Hospital because of marked hairiness of face and body of three years' duration, and amenorrhea.

Menstruation began at age of 17, was always scant, but regular for about one year, then stopped. Urine output and appetite normal. Examination on admission showed the patient to have a marked growth of hair on the face and over the body generally. She was not obese. Blood pressure 110/60; the fasting blood sugar was 71 mg. per cent, sugar tolerance curve normal. Basal metabolic rate +14, −1, +3. Blood cholesterol 87 mg. per cent; blood sodium 346 mg. per cent; blood potassium 19.1 mg. per cent; blood sodium chloride 634 mg. per cent. A right adrenal tumor was diagnosed with the aid of intravenous pyelography. The urine contained 8–10 times the normal amount of 17 ketosteroids (Dr. Willard Allen).

A tumor of the right adrenal gland the size of a large grapefruit was removed successfully after preoperative preparation with liberal amounts of adrenal cortical extract. After operation, the patient again required large amounts of whole adrenal cortical extract for several weeks to prevent collapse and hyperpyrexia. Her ultimate recovery was complete. Microscopic study of the tumor tissue showed it to be an adenoma of the adrenal cortex, few mitotic figures being present. For two years the patient has been well. Her menstruation is normal; blood pressure normal.

COMMENT: This patient did not show any of the signs and symptoms characteristic of Cushing's syndrome. The nature of the hormone secreted by the tumor was primarily androgenic; nevertheless, it must also have contained other factors necessary for life because of the large amount of whole adrenal cortical hormone indispensable after the operation for two weeks. Because the tumor did not produce polyuria and hypertension it apparently did not secrete an excess of the desoxycorticosterone fraction. The normal basal metabolic rate and the low blood cholesterol indicate further than the hormone did lead to changes in the glandular hypophysis characteristic of Cushing's syndrome.

BIBLIOGRAPHY

1 Cushing, Harvey: Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic Nervous System. Thomas. Springfield, Illinois, and Baltimore, Maryland. 1932.

2 Heinbecker, Peter: The Pathogenesis of Cushing's Syndrome. Medicine, **23**, 225–247, 1944.

3 Crooke, A. C.: Change in Basophil Cells of Pituitary Gland Common to Conditions which Exhibit Syndrome Attributed to Basophil Adenoma. J. Path. and Bact., **41**, 339–349, 1935.

4 Rasmussen, A. T.: Relation of Basophilic Cells of Human Hypophysis to Blood Pressure. Endocrinology, **20**, 673–678, 1936.

5 McQuarrie, I., Johnson, R. M., and Ziegler, M. R.: Plasma Electrolyte Disturbance in Patient with Hypercortico-adrenal Syndrome Contrasted with that found in Addison's Disease. Endocrinology, **21**, 762–772, 1937.

6 Ragan, C., Ferrabee, J. W., Phyfe, P., Atchley, D. W., and Loeb, R. F.: A Syndrome of Polydipsia and Polyuria Induced in Normal Animals by Desoxycorticosterone Acetate. Amer. J. Physiol., **131**, 73–78, 1940.

7 Mulinos, M. G., Spingarn, C. L., and Lojkin, M. E.: Desoxycorticosterone and Diabetes Insipidus-like Condition. Amer. J. Physiol., **135,** 102–112, 1941.

8 Mellgren, Jan: The Anterior Pituitary in Hyperfunction of the Adrenal Cortex. Acta Pathologica et Microbiologica Scandinavica, Supplementum LX. Ejnar Munksgaard, Kopenhagen, 1945.

9 McKeown, T., and Spurrell, W. R.: The Results of Adrenalectomy in the Pregnant Albino Rat. J. Physiol., **98,** 255–262, 1940.

10 Gaunt, R., and Hays, H. W.: The Life-maintaining Effect of Crystalline Progesterone in Adrenalectomized Ferrets. Science, **88,** 576, 1938.

11 Reynolds, S. R. M., and Allen, W. M.: Physiology of the Corpus Luteum. Amer. J. Obst. and Gynec., **30,** 309–318, 1935.

12 Norris, Edgar H.: Arrhenoblastoma. Amer. J. of Cancer, **32,** 1–29, 1938.

13 Zondek, B.: Clinical and Experimental Investigations on the Genital Functions and their Hormonal Regulation. Williams and Wilkins Co., Baltimore, 1941.

14 Leyton, O., Turnbull, H. M., and Bratton, A. B.: Primary Cancer of the Thymus, with Phariglandular Disturbance. J. Path. and Bact., **34,** 635–660, 1931.

15 Heinbecker, P., and White, H. L.: Hypothalamico-hypophysial System and its Relation to Water Balance in the Dog. Amer. J. of Physiol., **133,** 582–593, 1941.

16 Heinbecker, P., White, H. L., and Rolf, D.: Experimental Obesity in the Dog. Amer. J. Physiol., **141,** 549–565, 1944.

17 Price, W. H., Cori, C. F., and Colowick, S. P.: The Effect of Anterior Pituitary Extract and of Insulin on the Hexokinase Reaction. J. Biol. Chem., **160,** 633–634, 1945.

18 Heinbecker, P., and Rolf, Doris: Hypophysial Eosinophil Cell and Insulin Sensitivity. Amer. J. Physiol., **141,** 566–570, 1944.

19 Long, C. N. H., Katzen, B., and Fry, E. G.: Adrenal Cortex and Carbohydrate Metabolism. Endocrinology, **26,** 309–344, 1940.

ACUTE INTUSSUSCEPTION IN INFANTS AND CHILDREN

BRUCE M. HOGG, M.D., AND EDWARD J. DONOVAN, M.D.
NEW YORK, N. Y.

FROM THE BABIES HOSPITAL, NEW YORK CITY, N. Y.

ACUTE INTUSSUSCEPTION is the most important and one of the most serious surgical emergencies met with in infancy and early childhood. It has been called variously invagination, introsusception and intussusception, and as the name implies, consists of invagination of a segment of bowel into a distal contiguous segment. The former is known as the intussusceptum and the latter as the intussuscipiens.

The frequency of the disease as seen in The Babies Hospital during the past 19 years has been about one in every 300 admissions. The 123 cases reported in this series have, with one exception, been seen and treated by the attending and resident staff of The Babies Hospital during the years 1927 to 1945, inclusive.

Since the last series reported from this hospital by Bolling,[1] in 1923, the mortality rate has declined from 30 per cent to the present 13 per cent. This is encouraging progress, which seems to have been achieved by better treatment following hospitalization, because the duration of the disease before admission to the hospital has shown no appreciable decrease. It is unfortunate that a disorder with such clear-cut symptoms and physical findings should continue to be so belatedly recognized. That the time to hospitalization can be effectively reduced was shown by Clubbe[2] in the early part of this century, when he attained an average duration of 17 hours in a fairly large series by means of an intensive educational campaign directed at both the medical and nonmedical group. That this is true is further demonstrated by the fact that among the private patients in this group the average duration was 18 hours to hospitalization, compared to 33 hours for the ward cases. The complete lack of improvement in early recognition of this emergency condition in this community during the past years would imply that considerable benefit might be obtained by an effort to bring it more vividly to the attention of the medical public as well as the lay group, through "Well" Baby Clinics and Health Clinics.

No obvious cause for intussusception could be found in 83 per cent of the cases; in 11 per cent enlarged lymph nodes were described in the region of the ileocecal junction, and in the remaining 6 per cent the figures were made up roughly as follows: Meckel's diverticulum was found in four cases; cysts were found in three; and a polypus in one. The definite organic causes were divided equally between the age-groups below one year, and over one year.

The classification used in this report is that suggested by Clubbe,[2] and followed by Bolling[1]—(1) ileo-ileal, or enteric; (2) enterocolic, or the double type; (3) ileocecal; and (4) colic. Eighty-five per cent of the cases in this group were of the ileocecal type.

In considering the natural history of the disease it was found that the white and colored races were equally represented, according to hospital admissions; males predominated over females in the ratio of 1.9 to 1; 44 per cent of the children were wholly breast fed and almost all of them were taking solid food by the time they were four months old. Three patients in this series had a history of intussusception in immediate or closely related members of the family. Forty-five per cent of the cases occurred in the first child and an additional 20 per cent in the second child. The usual description of a healthy, well-developed infant was borne out by the finding that most patients fell within a normal weight limit for age and height. Characteristically, these children are healthy and have little which might be considered significant in their past history. In this series there were, however, 11 with a history of recent or fairly recent diarrhea, four with history of previous intussusception, and five with a history of allergy.

The outstanding features of the histories were: Acute onset, intermittent pain, vomiting, and a bloody bowel movement following the onset of the illness. It might be well to point out, however, that 20 per cent of the patients had perfectly normal bowel movements after the symptoms began. The most frequently noted physical findings were: Good nutrition and hydration, a palpable abdominal mass, and blood on rectal examination. About 30 per cent of the patients had increased temperatures and white counts above normal, although, in general, this information was not of much value except in the cases of marked elevations, when it was considered to be a poor prognostic sign.

In ten cases in which the barium enema was used as a diagnostic aid, it was positive, and in an additional case of the ileo-ileal type, abnormality in the region of the terminal ileum was suggested.

The average duration before admission for this group was 33 hours, and 44 per cent were seen within the first day of illness. It is discouraging to note that there has been no improvement in these figures when five-year groups are compared over the period studied. Twenty-five per cent of all children had been ill three days or longer; this is hard to understand when one considers that the patients are drawn from a large metropolitan population within easy reach of doctors and hospitals.

The age distribution placed 75 per cent of the cases in the ages three to 11 months, with one case less than one month old and three cases over four years of age. As noted previously, the yearly rate has been fairly constant and there has been no noticeable seasonal variation in incidence.

Because of the uncertainties attendant upon nonoperative treatment by carefully controlled barium enema and fluoroscopy, this method has been rarely used. In all, five patients were so treated; in one there was complete reduction and uneventful recovery took place; of the remaining four, in one there was failure within limits of what was considered safe pressure, and one promptly recurred with evacuation of the barium. The two remaining patients were operated upon because of some uncertainty as to the completeness of the reduction. One was found to have an ileo-ileal intussusception in the terminal

ileum, while the other was found to have been completely reduced by the barium. There were three instances of spontaneous reduction, one following an enema, and two following an anesthetic. One of the latter was operated upon and evidences of the intussusception were found. All three made uneventful recoveries.

In two nonoperative cases the diagnosis was made at autopsy; both of these were very young infants who were admitted to the hospital in poor condition, and one showed on postmortem an ileo-ileal intussusception, and the other a double jejunojejunal intussusception.

The increasing appreciation of the value of parenteral fluids and blood in the preoperative preparation of such cases is well-illustrated in this series. In fact, it seems to be the one addition to treatment which might be considered accountable for the diminution in the mortality rate. During the years 1927–1931 one-fifth of the patients received some form of preoperative fluid therapy, and the mortality rate was 20 per cent, whereas during the years 1941 to 1945 the mortality rate fell to 10 per cent, and almost half of the patients received preoperative supportive fluids. Postoperative therapy of this type has always been at a somewhat higher level, though it, too, has increased. The impression gained, however, is that in many instances it was too little, and too late. Too much importance cannot be attached to this form of therapy. All such cases should be brought into adequate fluid and blood volume status before, during and after the acute surgical phase of their treatment.

Another form of preoperative therapy which has been minimally used in this group is that of gastric or duodenal suction. Gastric lavage should always be done and continuous gastric suction instituted if distention exists.

The striking drop in mortality rate in acute intestinal obstruction in adults following the adequate use of these forms of therapy is well-known, and they should certainly not be neglected in such cases in children.

The operative technic has not changed much during the period studied, ether being the anesthesia of choice, and a paramedian right rectus muscle-splitting incision the one customarily employed. The intussusception is then gently reduced by milking from below, and the characteristic dimple and edema in the area of the cecum ironed-out by the use of hot packs and gentle pressure before the intestine is replaced into the abdomen. A layer-closure of the abdomen is always done, and the suture material most frequently used is chromic catgut, with usually two or three heavy silk retention sutures. Appendicectomy was performed in 13 cases; in three the appendix was found to be abnormal on pathologic examination. Generally speaking, appendicectomy is considered unwise unless, of course, the appendix appears grossly to be involved.

Nine cases required resection because of irreducibility, gangrene or perforation. In five of these, anastomosis was effected by the suture method, and in four by a Mikulicz procedure. In the cases done by suture there were three deaths and one survival under one year of age, and in the cases done by the Mikulicz procedure there were two deaths and two survivals under one year

of age. It would appear from this limited experience that there might be some virtue in the employment of the Mikulicz procedure, particularly in very young patients.[3, 4]

The postoperative course of the uncomplicated case is usually uneventful, though they may have a sharp temperature rise during the first two or three days, perhaps due to absorption of toxic products from the injured bowel. Feeding is usually not a problem, and the foul diarrhea mentioned by some authors[4] has not been noted in this group. The postoperative complications most frequently noted were shock, pneumonia, disruption, and obstruction.

Confirming the findings of others, 83 per cent of the cases showed no visible reason for the development of intussusception. The most frequently noted accompanying pathology was enlarged mesenteric lymph nodes. This finding was also noted by Wakeley and Atkinson,[5] and as a possible evidence of generalized lymphatic hyperplasia, would seem to lend credence to the theory that lymphatic hypertrophy in the region of the terminal ileum and ileocecal valve is an important etiologic factor in these cases. Six per cent of the cases showed some definite organic abnormality which was considered to be a precipitating factor; these were listed previously. Again, coinciding with the experience of others, 85 per cent of the cases were of the ileocecal type, 12 per cent of the enterocolic or double type, and 3 per cent of the entirely enteric variety. No instance was recorded in this series of a colocolic intussusception.

Wound-healing complications, as recorded, included four disruptions, with no fatalities, three trivial wound infections, and two serious wound infections, with one fatality.

There were 16 deaths, or an over-all mortality rate of 13 per cent. The average duration of the disease in these cases before hospitalization was three days, and over. The major causes of death are listed in the following order: shock, peritonitis, and pneumonia. In one death, which occurred in the operating room, the intussusception was complicated by a volvulus of the entire small intestine. Another death occurred on the 49th day, with recurrence of intussusception following an apparently successful resection. Two nonoperative deaths occurred in young infants who were admitted to the hospital in poor condition and with rather obscure histories; one of these cases was found at autopsy to have a double jejunojejunal intussusception, and the other an ileoileal intussusception. While the enteric and enterocolic types of intussusception constituted only 15 per cent of the group, the mortality rate in cases of this type was 55 per cent. The mortality rate tended to be higher in all types as the intussusception progressed toward the rectum.

There were two cases of what might be considered chronic intussusception, one of four weeks' duration and one of one week's duration. The diagnosis of partial intestinal obstruction was made roentgenologically, and confirmed at operation. Both were successfully reduced and made uneventful recoveries.

There were four cases of recurrent intussusception; with one exception the time to first recurrence was less than one year. One case recurred three times in nine years, and another twice in five years. These cases were all of

the ileocecal type, and no cause was found to account for the recurrent intussusception. In three cases, side-to-side suture of the portion of the terminal ileum to the ascending colon was done, twice on the occasion of the first recurrence. One of these cases subsequently had two recurrences, the other was apparently cured. The third case was so treated on the second recurrence, and had no further trouble. The fourth case received no preventive treatment, and has remained well. Though no conclusions can be drawn from this experience, in general, it is felt that preventive measures are of no avail.

There appear to be two main factors influencing the mortality rate in this condition; first, the duration of the disease; and second, the type of intussusception. The mortality rate in those cases seen in the first 24 hours was less than 2 per cent, whereas in those ill three days or longer it was 72 per cent. As noted previously, the enteric and the enterocolic type of intussusception, while comprising only 15 per cent of the total, carried a mortality rate of 55 per cent. Physical findings of poor prognostic import, and probably related to the above factors, were poor hydration, distention and elevated temperature. As noted previously, the mortality rate tended to increase in all types of intussusception as the intussusception progressed toward the rectum. The greater hazard inherent in the enteric and enterocolic types of intussusception is brought out further by figures indicating that resection was necessary in 21 per cent of these cases, and in only 4 per cent of the ileocecal type.

Sixty-one per cent of these cases have been followed in the clinic for an average of three years. Two of the group have small postoperative herniae, and two have symptoms which might be considered related to the disease, namely, repeated attacks of colic, and severe constipation.

SUMMARY AND CONCLUSIONS

(1) Figures relating to the natural history, signs, symptoms and pathology of this condition as reported by other authors[4, 5, 6] have, in general, been confirmed.

(2) Factors of poor prognostic significance in this series were found to be duration over 24 hours; the enteric, or enterocolic type; advanced progress toward the rectum of the intussusceptum; poor hydration; bowel distention; and elevated temperature.

(3) The time before hospitalization has not changed since the last series reported from this hospital 23 years ago. A plea is made for earlier recognition of this surgical emergency.

(4) It is concluded that the safest and surest treatment is surgical, although the experience with insufflation methods under fluoroscopic control has been limited.

(5) Fluid balance and blood volume should be restored and maintained during the preoperative and operative period by parenteral means, and continued during the postoperative course, as indicated. A more liberal use of such measures is urged.

(6) All cases should receive a gastric lavage preoperatively, and if abdom-

inal distention exists, continuous gastric or duodenal suction should be instituted.

(7) Nine cases of resection are reported, with a mortality of 55 per cent. It is suggested that a Mikulicz procedure may be of value in reducing the mortality, particularly in young infants.

(8) Follow-up data are given on 61 per cent of the cases followed for an average of three years.

REFERENCES

1 Bolling, R. W.: ANNALS OF SURGERY, **78**, 349, 1923.

2 Clubbe, C. P. B.: The Diagnosis and Treatment of Intussusception. New York Oxford University Press, 1921.

3 Woodhall, B.: Modified Double Enterostomy. Mikulicz, in "Radical Surgical Treatment of Intussusception in Children." Arch. Surg., **36**, 989-97, 1938.

4 Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood. W. B. Saunders Co., 1941.

5 Wakeley, C. P. G., and Atkinson, F. R. B.: Acute Intussusception in Children. Brit. J. Child. Dis., **35**, 241–50, 1938.

6 Close, H. G.: Acute Intussusception in Children: A Statistical Analysis of 363 Cases at Guy's Hospital. Guy's Hosp. Rep., Lond., **81**, 436–43, 1931.

PREVENTION OF WOUND INFECTION BY THE INJECTION OF NONTOXIC ANTIBACTERIAL SUBSTANCES*

EDWARD L. HOWES, M.D.

NEW YORK, N. Y.

FROM THE DEPARTMENT OF SURGERY, COLUMBIA UNIVERSITY, NEW YORK, N. Y.

IN A PREVIOUS PAPER,[1] a mixture of streptomycin, 200 units per cc., and sulfamylon, 5 per cent,† was demonstrated as being capable of killing a three-hour growth of bacteria on a blood agar plate. This combination destroyed a large variety of bacteria and mixed cultures. In fact, no resistant strains have been encountered thus far. All of the gram-negative bacteria were destroyed although *B. pyocyaneus* tended to grow back again over the area where the pseudomonas was previously destroyed.

This combination of streptomycin and sulfamylon was also demonstrated to be innocuous to tissues. When constantly in contact with adult tissue, cultures were only mildly inhibited in growth. The mixture did not produce hyperemia of the conjunctiva of the eye of the rabbit nor adhesions in the peritoneal cavity. When injected into muscle, neither leukocytosis nor fibrosis resulted. It did not retard the rate of wound healing.

This data suggested that the mixture of streptomycin and sulfamylon at these concentrations should be an ideal subcutaneous antiseptic. Thirty clinical cases were treated with the combination without untoward effects and without infection, but this group was too small to be of statistical significance. To prove the point that the combination would prevent infection in wounds, the experiments about to be described were undertaken. A method was previously devised in experimental animals of producing 100 per cent infected wounds. The failure of treatment of the resulting infection with other agents has been reported elsewhere.[2] This same method has now been employed to test the efficiency of the combination of streptomycin, 200 units per cc., and sulfamylon, 5 per cent, in preventing infection in the wound.

Method.—Under anesthesia, a defect 3 cm. square was cut in the skin of the back of the rabbit just lateral to the spinal column. The loose subcutaneous tissue and fascia were excised and the underlying muscle was vigorously crushed with a Kocher clamp. The wound was then contaminated with bacteria, either using floor dirt as the contaminant, or a 24-hour growth of a specific bacteria. Without débriding the crushed tissue, the wound was then treated with the combination of streptomycin and sulfamylon. The surface was washed with the combination and, in addition, 15 to 20 cc. were injected in the tissues about the wound. The wound was covered with vaselined gauze and a protective dressing and jacket applied to the animal. The control group of wounds received no treatment. They were covered with dry gauze.

* The work described in this paper was done under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Columbia University, New York, N. Y.

† Marfanil = homosulfanilamide = 4-amino, 2 methylbenzene sulfonamide hydrochloride. Merck furnished the streptomycin, Winthrop the sulfamylon.

The first group of animals was treated with streptomycin and sulfamylon immediately after the wound was made and contaminated. The second group was treated three hours after the wound was made and contaminated, and the third group was treated after an interval of 12 hours.

The wounds were inspected four days later to determine whether infection had occurred. A cotton swab was saturated with secretions from the wound and this was smeared on a blood agar plate and incubated for 24 hours to

TABLE I

Rabbit No.	Contaminated With	Treatment	Gross Appearance After 4 Days	Blood Plate Culture on 4th Day
		UNTREATED CONTROLS		
640	Floor dirt	None	Grossly infected	Good growth of bacteria
642	*Staph.* culture	None	Wound very dry and necrotic	Thick culture of *Staph.*
644	*Staph.* culture	None. Vaselined gauze	Wound full of pus	Thick culture
648	Floor dirt	None. Vaselined gauze	Wound full of exudate	Good growth of bacteria
660	Floor dirt	None. Vaselined gauze	Wound full of dead tissue and pus	Good growth of bacteria
		TREATED SERIES		
641	Floor dirt	Immediate treatment with streptomycin mixture	Wound quite clean	No growth
643	*Staph.* culture	Immediate treatment with streptomycin mixture	Tissues, in general, healthy. Good healing obtained later	Scattered colonies
649	Floor dirt	Immediate treatment with streptomycin mixture	Clear bloody exudate. Edematous connective tissue	Two or three colonies
650	Floor dirt	Immediate treatment with streptomycin mixture	Wound clean and moist	No growth
659	Floor dirt	Immediate treatment with streptomycin mixture	Healthy and red, with some dead tissue	One colony
		DELAYED TREATMENT		
645	*Staph.* culture	3 hrs. after trauma with streptomycin mixture	Considerable pus	Good growth of bacteria
646	*Staph.* culture	3 hrs. after trauma with streptomycin mixture	A little pus and dead white tissue	Thickly scattered colonies, 200+
647	Floor dirt	3 hrs. after trauma with streptomycin mixture	Dead tissue and pus under skin edges	Good growth of bacteria
656	Floor dirt	24 hrs. after trauma débrided and treated with streptomycin mixture	No gross pus	No growth
651	Floor dirt	4 hrs. after trauma débrided and treated with streptomycin mixture	No gross pus	One colony

determine the quantity of bacterial contamination. A direct smear was also made and this was given a Gram stain. Color photographs were taken of the wound to record the character of the healing. The amount of exudate and the appearance of the tissues were noted. The rate of healing was not studied.

Both the wounds which became infected and those that did not were subsequently treated with the combination of antibacterials to determine whether a more rapid resolution of the established localized infection occurred and if continuing protection took place.

Results.—The five wounds treated immediately with the mixture of sulfa-

mylon and streptomycin remained free of infection on the fourth day, while the five wounds that were not treated were filled with pus (Table I). The blood plates made from the nontreated wounds showed heavy concentrations of bacteria (Fig. 1). On the contrary, those made from the treated wounds showed only occasional colonies of bacteria or no growth (Figs. 2 and 3). The tissues of the nontreated wounds were gray and necrotic and appeared frankly infected (Fig. 4). The tissues of the treated wounds showed no infection. They were bright red and the crushed tissue had disappeared (Fig. 5). A small amount of clear fluid was present. Granulations were absent, as is usually the case in this specie of animals in this particular anatomic location. Direct smears taken from both groups of wounds showed the following contrasts: In those taken from the wounds which became infected, every leukocyte contained many bacteria and there were many extracellular micro-organisms as well. In the smears taken from the treated wounds wherein infection was prevented, numerous leukocytes were also present but only an occasional one contained bacteria, and none were extracellular.

Additional treatment of both the infected and the noninfected wounds with the antibacterials yielded the following results. Neither injection nor washing caused resolution of infection although the bacteria remained susceptible to the action of the streptomycin and sulfamylon. To the contrary, wounds in which infection had been prevented remained uninfected regardless of whether the subsequent treatment was with the combination of antibacterial substances or with vaselined gauze or with dry dressing. The tissues in these wounds continued to be bright red. Rapid contracture of the surrounding tissues and regeneration of new tissues subsequently took place. In other words, when infection was originally prevented, the wound continued to heal without evidence of infection while if the wound became infected, antibacterial substances did not cause resolution even though the bacteria remained susceptible to the antibacterial agent. Figure 6 shows that the wound in which infection was prevented was almost healed on the 15th day. Figure 7 shows that contraction also took place in the infected wound although pus and slough were still present eight days later. Figure 8 shows a bacterial smear taken two hours after treatment with the combination of antibacterial substances. Many bacteria are still present in spite of treatment with the potent antibacterial mixture.

In contrast to the success obtained in preventing infection of wounds in the presence of crushed tissue by immediate treatment with the combination of streptomycin and sulfamylon, infection occurred when wounds were treated three hours after infliction and contamination. One wound appeared to be reasonably free of infection, yet it contained considerable fluid and the blood plate showed a large number of bacterial colonies. The other four wounds were definitely infected and their blood plates were characteristic. The recovered bacteria remained susceptible to the combination of antibacterials and, hence, an increased resistance to the action of the mixture would not account for the failure to prevent infection. As was expected, blood smears taken from the wounds, three hours after contamination, showed that there were really fewer

bacteria on the surface of the wound than when it was first contaminated. An abundance of the mixture was used to wash the tissues and was injected and, therefore, the presence of too many bacteria did not seem to be a logical explanation of the lack of success in controlling infection. In an attempt to find an

FIG. 1 FIG. 2

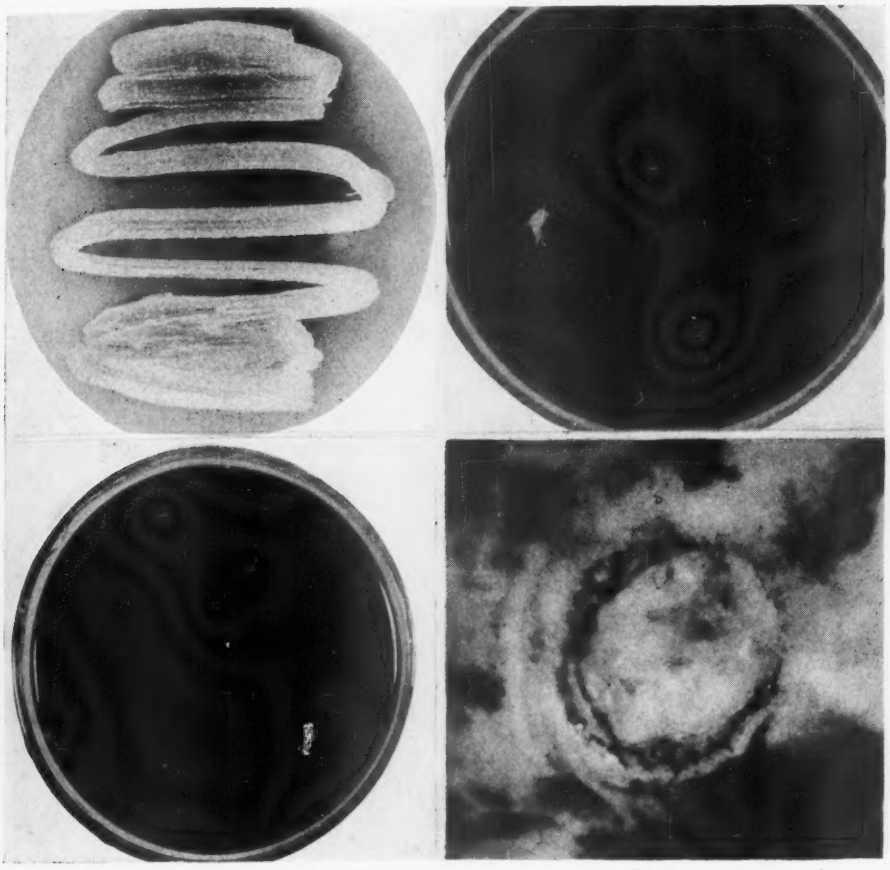


FIG. 3 FIG. 4

FIG. 1.—Blood plate—infected wound.
FIG. 2.—Blood plate—treated wound.
FIG. 3.—Blood plate—treated wound.
FIG. 4.—Gross appearance—infected wound, 4 days.

explanation, biopsies were taken of the loose connective tissues directly under the skin and of the muscle. Microscopic examination showed that many leukocytes had already invaded the tissues and every leukocyte contained many bacteria.

The combination of streptomycin and sulfamylon also failed to prevent infection from developing when treatment was given 12 hours after infliction

and contamination of the wound. Again, the bacteria remained susceptible to the action of the combination, although now there was a definite increase in their numbers and, again, examination of the tissues showed that there were many leukocytes present which contained bacteria. Moreover, some of the bacteria were extracellular.

FIG. 5 FIG. 6

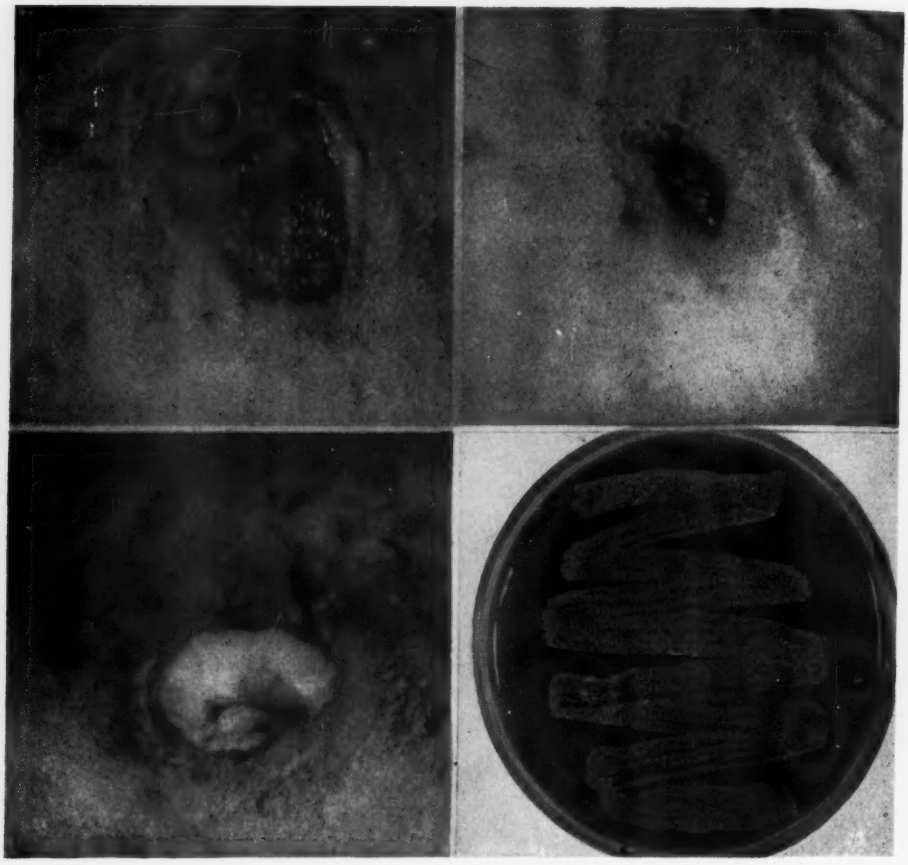


FIG. 7 FIG. 8

FIG. 5.—Gross appearance—treated wound, 4 days.
FIG. 6.—Treated wound—15th day.
FIG. 7.—Nontreated wound—8th day.
FIG. 8.—Blood plate—infected wound, 2 hours after treatment.

One of the three-hour wounds and one of the 12-hour wounds were treated by débridement and irrigation and were injected with the combination of streptomycin and sulfamylon. Infection was prevented in both wounds.

DISCUSSION.—Without a pronounced increase in the number of bacteria in the wound, with the bacteria remaining susceptible *in vitro* to the action of the antibacterials and with the amount of traumatized tissue unchanged, some other

reason must be found to explain why infection was not prevented when the wound was treated three hours after injury.

There is the possibility that the micro-organisms had located deeper in the tissues. Failure of prevention of infection has often been explained on the basis that bacteria deep in tissues are not contacted by solutions washing the surface of the wound, and, for this reason, the method of injecting the solution was originally adopted, apparently with success, immediately after injury. Lack of prevention later is difficult to explain on the same basis, therefore, if the bacteria remained extracellular. Only one other possible explanation can be offered; namely, that the extracellular fluid clotted and with the deposition of fibrin the diffusion of the antibacterial solution was prevented throughout the area. Dilution of the concentration of streptomycin and sulfamylon by edema fluid does not seem to be the answer because an excessive amount of solution was used.

The most logical explanation of the failure to prevent infection of the wound after three hours is, that many of the bacteria were no longer extracellular, and the antibacterial substances failed to contact them. Phagocytosis of the bacteria by the leukocytes placed the micro-organisms within cells. Both Wright[3] and Flemming[4] showed that ingestion by leukocytes does not always destroy bacteria. They made cultures from pus obtained from wounds and demonstrated that their contained bacteria grew on the surface of smeared blood plates. On the other hand, "sterile" leukocytes recovered from the pleural cavity in response to aleuranot, contained an antibacterial substance which prevented the growth of bacteria smeared on blood plates.

Thus, while phagocytosis is helpful in combatting infection, yet, if the leukocyte is killed before the bacteria are destroyed the micro-organisms are free to contaminate the wound again. Flemming believes, for example, that leukocytes, wandering to the surface of wounds, die and undoubtedly leukocytes are killed in many ways during the exudative phase of healing. If, therefore, destruction of bacteria by the leukocytes can not be relied upon and antibacterial substances must be used to kill them, then the leukocytes must be penetrated by the solution. If the leukocyte is dead, this is difficult to accomplish and the leukocytes will be killed unless the substance has a special selective action against the micro-organism.

The three-hour period was selected at random. Consequently, no statement can be made as to whether the combination of antibacterial substances would fail if used within this interval. On the other hand, failure certainly continues after three hours, for phagocytosis continues and new difficulties are added. The number of bacteria increase after four or five hours and they invade tissues and cause putrefactive necrosis. This necrotic tissue not only shields the bacteria from the action of the antibacterial substance, but also provides ready nutrition for those surviving. On the other hand, a wound free of dead tissue is not fertile soil for the remaining micro-organisms to propagate again. From the experimental viewpoint, it is perhaps fortunate that one element of the problem can be studied as early as three hours after injury.

The failure of streptomycin and sulfamylon to hasten the resolution of the established infection recalls that penicillin and the sulfonamides, although they did prevent spread of infection from the wound, also failed, regardless of whether they were used locally or generally. The sulfonamides failed partly because they were only bacteriostatic, acted slowly and, like penicillin, did not inhibit the growth of gram-negative bacilli that are also capable of producing pus. Inadequacy of antibacterial action cannot be used as an excuse for the failure of the combination of streptomycin and sulfamylon however, and, hence, the contention is strengthened, that resolution of an established infection requires in addition to a potent bacteriocide, adjunct chemotherapy; to dissolve slough, to explode leukocytes, and to provide chemical drainage. This need has been discussed elsewhere.[5]

While streptomycin and sulfamylon, applied immediately, were used to prevent infection in these experiments, other antibacterial substances can be substituted if they possess the required properties which allows them to be injected. These are, that the substance will kill bacteria in the presence of blood and serum in a bacteriocidal concentration that will not destroy tissues nor cause exudation. In addition, the substance must possess a wide range of bacteriocidal activity, act quickly, and be free of general toxicity. Penicillin, for example, can be substituted as an antibacterial to destroy gram-positive cocci and bacilli, but another one would have to be used with it to destroy the gram-negative bacilli. Some of the new antibiotics now being developed will undoubtedly qualify.

No attempt has been made to employ either streptomycin or sulfamylon alone. They were combined originally with the thought that their antibacterial activity would complement each other. If either one were used alone, sulfamylon 5 per cent seems the most likely one to select because streptomycin has weak action against the green and hemolytic streptococci and sulfamylon has proven effectiveness against anaerobic bacteria.

A word of caution must be said about the clinical use of these antibacterials to prevent infection in wounds. They, and the method of employment, must not be substituted for good surgery. Although infection was prevented by immediate treatment in the presence of traumatized tissue in the experimental wounds, dead tissue is a powerful member of the trio which produces infection in wounds and should be removed as completely as possible because no evidence was produced that the mixture would prevent infection caused by contaminated foreign bodies left in the presence of dead tissue. Foreign bodies as the second member of the trio which produces infection should always be removed. On the other hand, the experiments do demonstrate that these antibacterials will prevent infection when some traumatized tissue is present and, therefore, when complete removal of traumatized tissue is not always possible, the use of this combination adds a measure of security which cannot be omitted. Further, the use of this combination to prevent infection in contaminated wounds containing a minimal amount of traumatized tissue and foreign bodies should be invaluable, for example, to wash the clean contaminated

operative wound, made to remove the diseased appendix, or for a large bowel resection. The line of anastomosis can be swabbed repeatedly with the solution without fear of creating adhesions.[1] Its use for first-aid, to cleanse small traumatic wounds, not containing either foreign bodies or dead tissue, can certainly be highly recommended for immediate treatment in place of so-called "antiseptics" that usually destroy tissues as well.

The problems of extending the usefulness of the mixture of streptomycin and sulfamylon in preventing infection beyond the three-hour period is now being studied.

CONCLUSIONS

(1) Sulfamylon, 5 per cent, and streptomycin, 200 units per cc., prevented infection in crushed wounds of five rabbits. All five control wounds became infected. No attempt was made to débride the excessive amount of traumatized tissue present. The wounds were washed and the surrounding tissues were injected with 20 cc. of the combination of antibacterial substances. The treatment was carried out immediately after infliction and contamination of the wound.

(2) On the other hand, the combination of sulfamylon and streptomycin failed to prevent infection in five experimental wounds treated three hours after infliction and contamination of the wound.

(3) The inclusion of the bacteria within leukocytes is offered as a possible explanation for the protection of the bacteria against the action of the antibacterials after three hours. *In vitro* tests showed that they were still susceptible to the action of the antibacterial substances. Failing to penetrate to the bacteria within the leukocyte, the cell may subsequently die and liberate them unharmed to recontaminate the wound.

(4) Repeated injections and washing of the wound with an established localized infection did not hasten resolution of the process of suppuration although the bacteria were susceptible to the *in vitro* action of the mixture. Pus in these wounds also contains bacteria with leukocytes where they would not be contacted.

(5) If this combination of antibacterial substances is used clinically to prevent infection in wounds, the principles of good surgery should not be neglected. Use should be limited to contaminated wounds, relatively free of traumatized tissue and foreign bodies.

(6) Other antibacterials can be substituted for the sulfamylon and streptomycin to prevent infection by immediate treatment if they kill bacteria quickly in the presence of blood, have a wide range of activity, do not destroy or irritate tissue at the bactericidal concentration and are nontoxic.

(7) Injection of antiseptic substances locally points to new possibilities in the local treatment of wounds.

REFERENCES

[1] Howes, Edward L.: Local Chemotherapy of Wounds: Tissue Toxicity of Certain Antibacterial Substances. Surgery, Gynecology, and Obstetrics. Accepted for publication.

[2] Howes, Edward L.: Treatment of Experimental Infected Wounds. Delivered at Meetings of Subcommittee of Infected Wounds and Burns, National Research Council, March 22, 1944 and December 8, 1944.

[3] Wright, Sir Almoth: The Study of Emigration and the Bacterial Effects Exerted in the Wound by Leukocytes. Lancet, **1**, 129, 1918. Also, Treatment of War Wounds. Lancet, **1**, 939, 1917.

[4] Flemming, Alexander: The Action of Chemical and Physiological Antiseptics in a Septic Wound. British Journal of Surgery, **74**, 99, 1919–1920.

[5] Howes, Edward L.: The Chemical Separation of Slough. In print.

A STUDY IN ARTICULAR REPLACEMENT

STEPHEN S. HUDACK, M.D.
NEW YORK, N. Y.

FROM THE DEPARTMENT OF SURGERY, COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, AND THE FRACTURE DIVISION, PRESBYTERIAN HOSPITAL, NEW YORK, N. Y.

THE PROBLEM of degenerative disease in articulations, either weight-bearing or not, is one which still challenges the surgeon. How to alleviate the pain and how to restore to use a painful stiff joint, due to degenerative disease, are questions which as yet have not been answered. It is not so simple as replacing caries in teeth, although some may consider that there is a rough parallelism. It is not simply a matter of prosthesis either, nor can it be simple substitution. Although the replacement idea is attractive so far it has not been adequately developed. Fundamentally, the idea may be seen as sound if the dynamic interrelationship between the host site and the replacement donor material were understood and, within useful limits, controlled.

The substitution for a degenerating articular surface of fascia and other soft-tissue materials cannot be compared to that of the cup arthroplasties[1] because the fascial replacement is temporary and the degree of survival of the donor tissue cannot be controlled. Conversely, though the arthroplastic cup is nonabsorbable it maintains an ever-shifting relationship to the host tissue, and cannot be considered to be a replacement but rather a substitution for the articular surface. The union, so to speak, of the donor to the host never takes place. In the fascial arthroplasties there is early death of the donor tissue; where the nonabsorbable cup is used the relationship of the donor element, particularly toward the head, is unstable.[2] The idea that with movement of the donor cup no single area of the host bone is subjected to sufficient strain to cause local death, is extremely attractive but clinical application of the idea has shown it to be only partially and temporarily successful. Perhaps if the cup moved in the hip socket and was fixed to the neck a more stable equilibrium of the joint could be established.

An experiment was planned to study a situation in which the weight-bearing strain of the donor element of the joint sought and reached a stable equilibrium with the host tissue of the moving part. The donor part was of course mobile on the torso element of the joint.

Perhaps for this experiment vitallium may have been a more suitable material.[3] However, chrome nickel steel alloy was used because it had been employed previously in the problem of open reduction and fixation of fractures.[4] Fixation of the donor element was considered from the point of view that: (a) Maximum weight-bearing surface be attained in the host tissue; (b) some limited adaptability of position to the host tissue should be present; (c) minimum injury to the circulatory supply of the host tissue be inflicted; and (d) the motor forces controlling the joint be maintained in normal dynamic balance insofar as possible.

The flanged nail fixation was adopted. It was seated into the medullary canal to control torque and transverse stress but a maximum surface was used for the weight-bearing plateau. For reasons of experimental expediency, the dog's shoulder joint seemed most suitable. As a weight-bearing joint it was accessible without great trauma to the soft-part attachments. The same cannot be said for the hip joint in the dog.

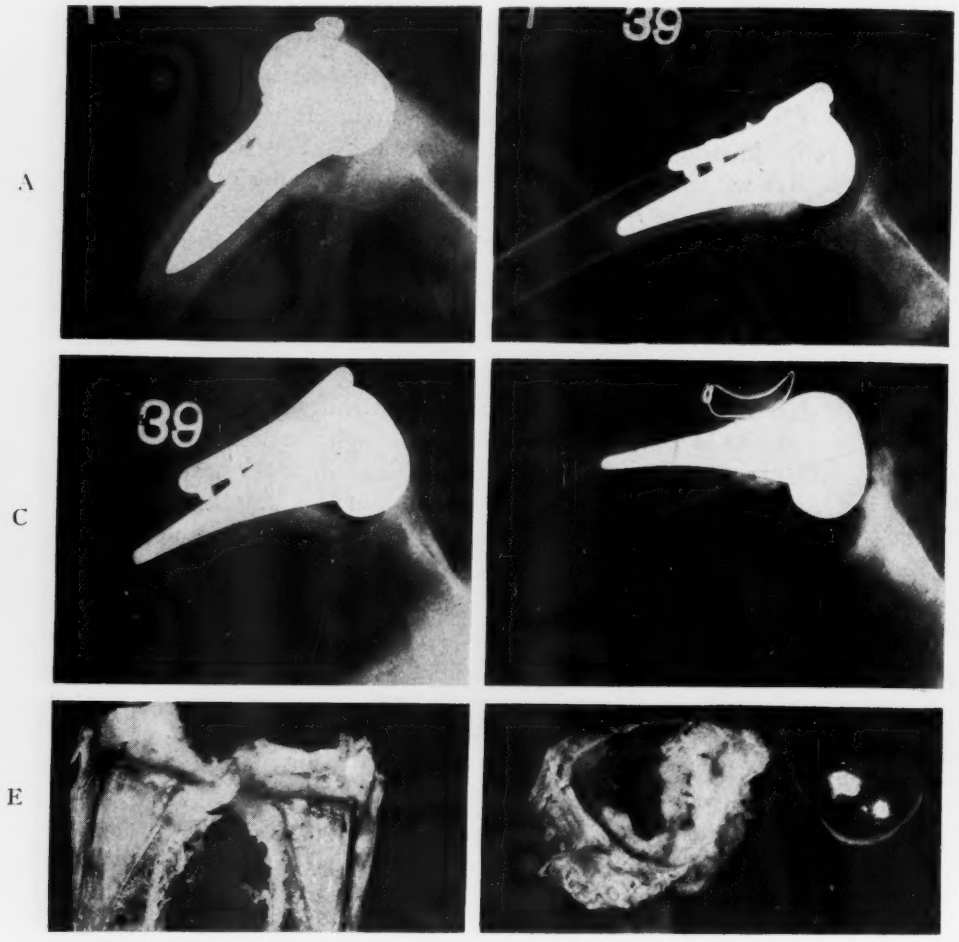


FIG. 1.—Roentgenograms of four shoulders five to ten months postoperative. The gross specimen of one of these, No. 15789 is shown after removal; five years and eight months postoperative.

A series of six dogs was employed. When certain technical difficulties were overcome, it was found that the animals, after operation, regained function to a limited degree in four weeks and thereafter progressed satisfactorily. By three months, almost full use was attained. There remained a residual limitation of motion depending on the technical success of the operation and other minor factors. The weight of the animal did not appear to be an important factor.

The first animal, though successful surgically, died of postoperative pneumonia. One of the others in which the greater tuberosity was not removed but in which a transcapsular approach was used, dislocated when the external rotator cuff pulled out the sutures and had to be sacrificed. The other four

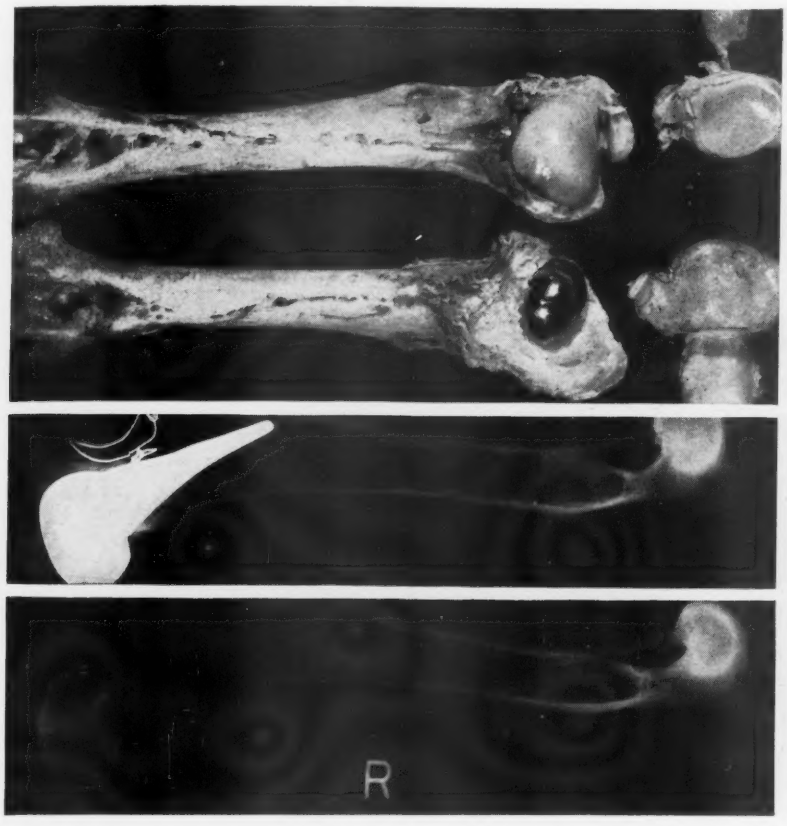


FIG. 2.—The operated and unoperated humerus and glenoid five years and eight months postoperative.

animals are referred to in Figure 1, upper roentgenograms. Three animals survived the operation well over six months. All the animals were active within four days of the operation. Except for one (Figure 1, upper left) they attained full activity in three months. Even the animal which developed osteomyelitis was active and bearing weight in three months, but it was obvious by comparison with the others that there was pain and limitation of use. When it was clear that the surgical procedure was feasible and accomplished the intended purpose of attaining function with a humeral head which had been replaced, the animals except the five-year survival were sacrificed. This latter animal is reported in the following protocol:

EXPERIMENTAL

Protocol of Dog.—Number 15789: Black and white male hound, weighing 39 pounds, somewhat underweight because he was convalescing from distemper. Operated June 6, 1940. Dr. Frank Nobiletti assisting.

For application of the replacement element to the right shoulder under nembutal anesthesia, the right shoulder was explored. The skin was separated-off with towels. The anterior margin of the deltoid was detached and the muscle retracted posteriorly. Some of the upper limits of the pectoral and subscapularis muscle attachments were separated to allow access to the upper humeral shaft. The external rotator cuff was detached with the greater tuberosity and retracted. A step-cut block of the upper humeral shaft was carried with the greater tuberosity to make anatomic reattachment of the greater tuberosity simpler.

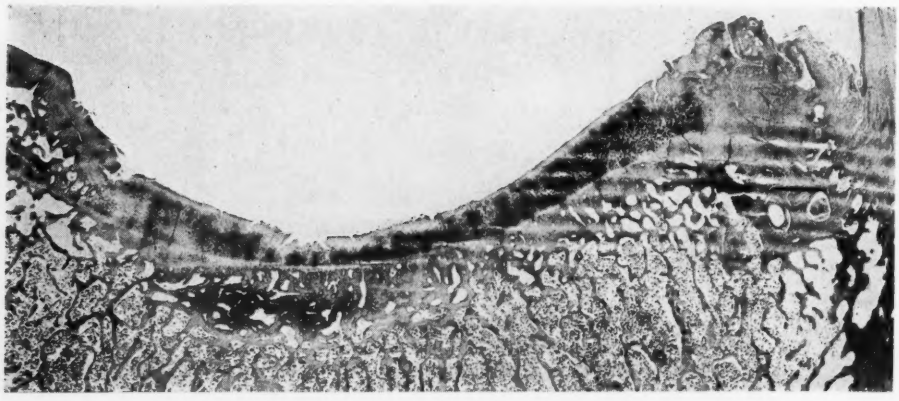


FIG. 3.—A low power field of the glenoid cavity.

The humeral head was then excised at the anatomic neck intracapsularly where the head meets the slightly expanded upper portion of the shaft. There remained a plateau of fairly dense cancellous bone. This plateau was marked with the flanged nail and the channel for the nail portion was partially formed with the use of a thin narrow osteotome. The donor element was then seated firmly into place and the shoulder was reduced.

The greater tuberosity was replaced and sutured through small drill holes with a mattress of No. .010-inch high chrome, low nickel wire.

The conjoint cuff and capsule were repaired and the wound was closed in anatomic layers. The skin was closed with vertical mattress sutures of "c" silk. Hemostasis was adequate but not absolute.

Postoperative Course.—The 1st postoperative day was eased by the use of morphine. The animal was quiet and ate very little. The wound showed considerable edema. By 48 hours, though still having pain, the animal was more comfortable. His appetite was fair, and the wound appeared clean. By the 4th postoperative day the dog had become livelier, touching his foot to the ground. His condition remained good, and by the 10th postoperative day the wound was healed and he was hopping around actively on three legs.

There was no essential change until the 30th postoperative day, when it was noted that the animal was bearing weight on the operated leg occasionally. He appeared in excellent health and ten days later was found consistently bearing weight on all four extremities. Forty-eight days postoperatively, although there was considerable atrophy of the shoulder girdle muscles, the dog was in excellent spirits bearing full weight and quite active. Indoor movies were taken of his activity.

By three months postoperatively, to an unprejudiced observer, the animal was completely normal. Careful clinical examination revealed, however, that there was some residual atrophy and, motion in all planes was reduced about 10 per cent. Outdoor movies taken at this time showed a normal running gait, and the dog could be made to jump from a four foot wall. This he did repeatedly, landing on his fore paws without appearing to favor the operated extremity.

A year later, except for a slight prominence of the greater tuberosity masked by his pelt, it was impossible to tell by the dog's activity that he had been operated upon. The atrophy had completely disappeared. He became a laboratory pet. About this time

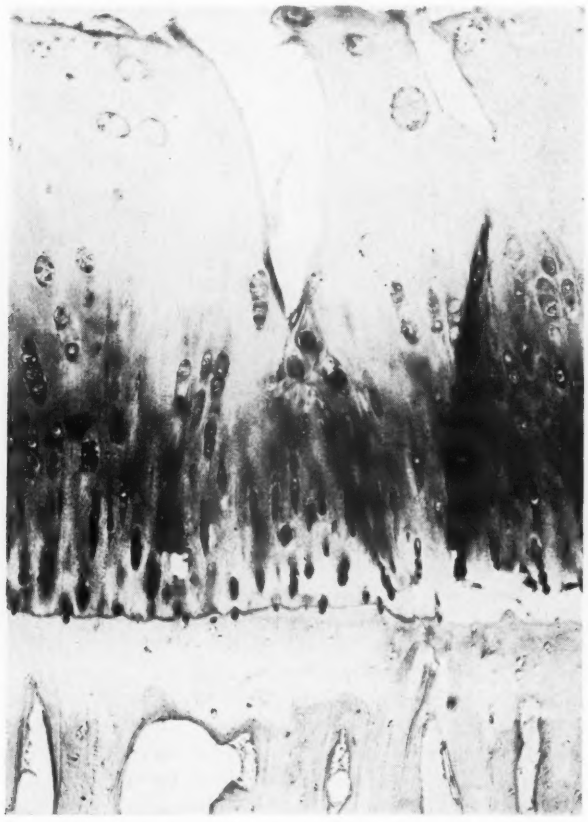


FIG. 4.—A higher power of the articular surface of the glenoid cavity shown in Figure 3.

(August, 1941) the author joined the armed forces and the care and observation fell to the animal operating room supervisor, Miss Daisy Mapes, who performed her duties superbly. The animal was mated to a suitable laboratory companion, but this concession to his welfare and happiness seemed ill advised because after long celibacy this unaccustomed activity almost prostrated the poor beast.

Nevertheless, he continued in good condition. Upon the author's return to civil duties (October, 1945), the dog was carefully examined both with and without anesthesia. This examination was five years and four months after the replacement in the right shoulder. Clinically, the dog was doing well. He had gained weight and his coat was thick. He

ran and chased without impediment. Close examination revealed that the limitation of motion had increased although this could not be detected by watching the animal's activity.

Forward extension of the shoulder as compared with its fellow was reduced about 20 per cent. External and internal rotation were reduced about 50 per cent. Caudal flexion of the shoulder was reduced about 25 per cent. There was a fine crepitation present on forced passive movement, which apparently was not painful. There were clinical indications that a degenerative arthritis was present. A roentgenogram, taken on November 29, 1945, showed that although the joint space was clear, there was evidence of periarticular proliferation.

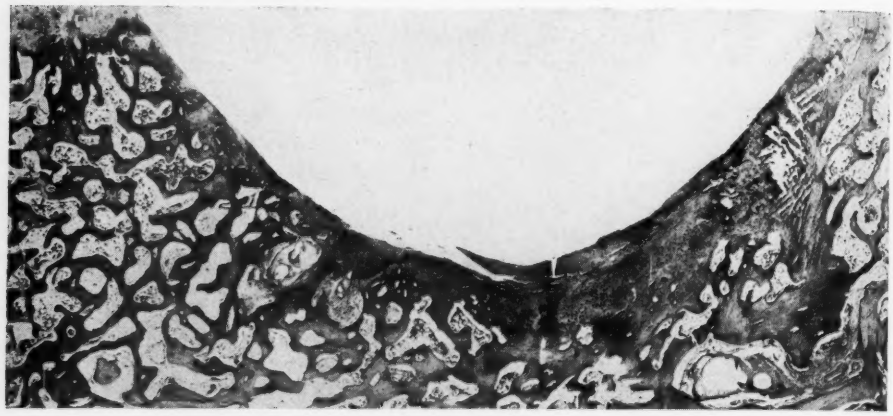


FIG. 5.—A low power field of the adaptive tissue near the greater tuberosity.

Postmortem Examination.—January 7, 1946: *Gross:* Condition of the muscles was good. There was no atrophy of the deltoid or trapezius. The infraspinatus was slightly atrophied. The insertion of the subscapularis muscle had migrated slightly distally. There was some heaping-up of the margins of the groove of the long biceps tendon but the binding down of the tendon and the lessening of mobility was slight. The tendon body appeared slightly flattened where it passed over the smooth metallic humeral head, otherwise not abnormal. The joint capsule, as a whole, was thickened and there was a small amount of synovial fluid present, which appeared normal.

On entering the joint the donor element appeared smooth, shiny, and uncorroded. The glenoid cartilage did not appear so smooth, as on the normal side. There was some lipping of the glenoid margin in the upper half with almost none in the lower margin. The hypertrophic tissue of the glenoid margins made the glenoid appear slightly deeper than on the normal side. There was some synovial membrane thickening, less in the inferior portion than elsewhere. The greater tuberosity was considerably hypertrophied and had partly overgrown the lateral part of the metallic element. This hypertrophy was enough so that abduction and rotation were limited because the greater tuberosity almost impinged on the tip of the spinous process of the scapula.

Adaptation of the Humerus.—The replacement element was smooth and very firmly seated in the humerus. The overgrowth by the greater tuberosity and firm seating in the humerus made removal of the prosthesis difficult. When removed, the adapted part of the humeral shaft showed a smooth, glistening fibrous membrane such as one sees beneath the surface of a stainless steel plate well-applied to bone. Beneath the fibrous membrane, there appeared a smoothly adapted layer of bone, no longer cancellous but appearing now to be of homogeneous density. There was noe spot of discoloration. This was a region about three millimeters in diameter where the three-flanged nail element meets the weight-bearing part of the head (Fig. 1, gross specimen).

TEXT DESCRIPTION OF FIGURES

Fig. 1.—(Upper left) shows roentgenograms of dog No. 15321, taken five months and ten days postoperatively. The operation was unsuccessful. The animal developed an osteomyelitis.

Fig. 1.—(Upper right) shows roentgenograms of dog No. 15329, taken five months and eight days postoperatively. Clinically, there was full use.

Fig. 1.—(Middle left) shows roentgenograms of dog No. 15328, taken five months and eight days postoperatively. The donor element is adapted. The animal was completely active but clinical examination showed considerable limitation of motion. The latter two animals had for fixation of the greater tuberosity, a small four screw plate.

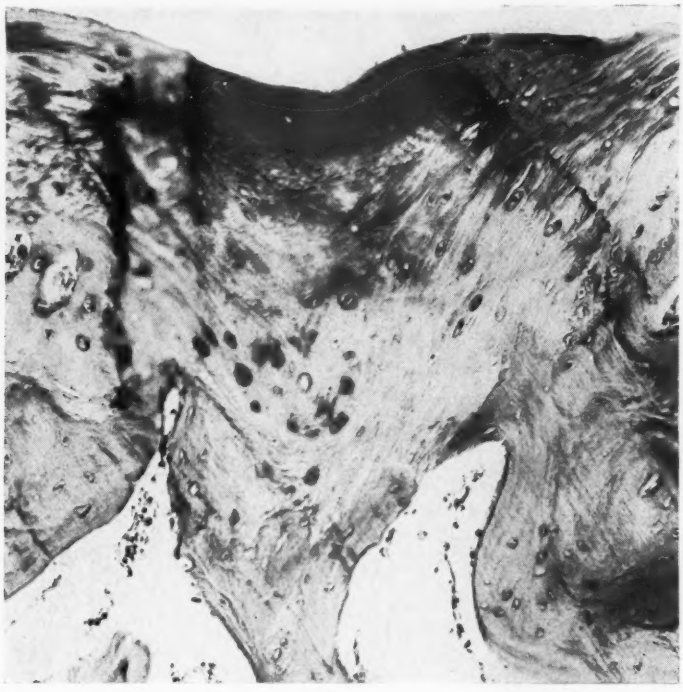


FIG. 6.—A higher power field of Figure 5 to show type of tissue.

Fig. 1.—(Middle right) shows roentgenograms of dog No. 15789, taken ten months postoperatively. The gross specimens are of the same shoulder four years and eight months later. (See protocol).

Fig. 2.—(Upper) shows the same humerus as in Figure 1 (middle right) four years and ten months later after removal. The articular surface of the glenoid is likewise shown with the normal side below it.

Fig. 2.—(Lower) shows roentgenograms of the humeri of the same animal, again, taken after removal following sacrifice.

Fig. 3.—Shows a low power field of the glenoid. Note the lipping of the lower margin of the glenoid with trabeculae forming over the articular cartilage and another articular surface superposed. At the upper limit where the long biceps tendon attaches there is some irregular cartilage production blending with some very dense fibrous tissue, poorly cellular. The supporting bone trabeculae in the middle portion are denser, thicker, and have few marrow cells.

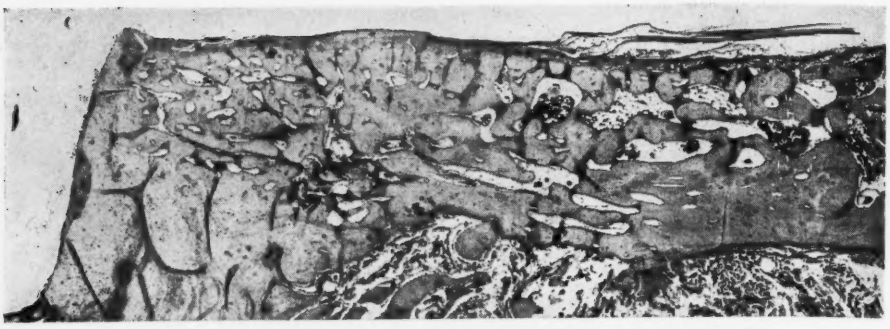


FIG. 7.—A low power field of the tissue at the junction of the weight-bearing surface and flanged nail fixation surface.

FIG. 8.—A higher power field of the junction area shown in Figure 7.

Fig. 4.—Shows a higher power of the central region where the cartilage was in the poorest condition. Note the thickened trabeculae and low cellular content of the marrow spaces.

Fig. 5.—Low power field in region of the greater tuberosity to show adaptation of a nonweight-bearing part of the humerus to the donor element. There are incompletely formed haversian units in which the lamellar structure is unevenly developed.

Fig. 6.—The tissue shown here is the same as in Figure 5 at higher magnification. Again, there is present a dense fibrocartilaginous tissue adjacent to a nonweight-bearing portion of the head. The trabecular support is not so heavy as in the weight-bearing part.

Fig. 7.—A low power field shows the region of the supporting structures where the flanged nail joins the weight-bearing surface of the head of the donor element. The pin portion shows an adaptive layer of dense lamellated fibrous tissue supported by heavy trabeculae. The weight-bearing portion shows a dense fibrocartilaginous adaptation.

Fig. 8.—The corner region of tissue in Figure 7 is here shown at higher magnification. There are no inflammatory cells present. The supporting bone trabeculae are quite heavy. The marrow spaces are not very cellular.

Fig. 9.—A region of the tissue surrounding the edge of the flanged nail. The separation of the dense fibrous layer from the underlying bone is an artefact. Before preparation for sectioning the fibrous and osseous layers were closely applied. Observe that there is no fibrocartilaginous reaction. The areolar tissue fills in the irregularities of the bone trabeculae. There are no signs of irritation or foreign body reaction. There are no inflammatory cells present.

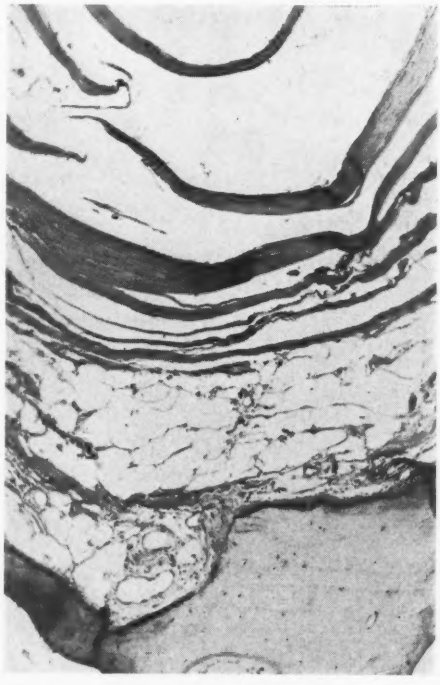


FIG. 9.—The tissue about the edge of a nail flange.

Fig. 10.—A cross-section of the dense fibrous tissue which is the lining membrane surrounding the flanged nail. It is poorly cellular and poorly vascularized. The lamellae separated away easily and it was impossible to keep attached to the underlying bone trabeculae. This tissue is very similar to the lining membrane shown in Figure 9 around the edge of a flange in the nail.

DISCUSSION.—There appear to be three types of adaptive tissue surrounding the donor element. The tissue surrounding the nonweight-bearing part of the flanged nail is a dense stratified connective tissue lying on flattened bone trabeculae. It acts as a fibrous envelope and is relatively acellular and poorly vascularized. There are no inflammatory cells in it.

Where there is weight-bearing with compression stress the adaptive tissue is more fibrocartilaginous. Its character varies somewhat depending upon the supportive trabeculae.

Regions in which there is more stress than in the supportive tissue around

the flanged nail, as in the region of the greater tuberosity, the fibrous and fibrocartilaginous elements combine, the fibrocartilaginous elements dominating somewhat. Foreign body response and inflammatory tissue is singularly absent.

Grossly, the fibrous envelope about the flanged nail resembles the tissue

FIG. 10.—Stratified fibrous tissue surrounding flanged nail.

one sees in the pin tract of pinned hips in which the pin is removed after healing has taken place.[5]

Although these experiments are fragmentary and incomplete because of the interruption of war, they may be considered as pilot experiments in the study of the adaptive capacity of cancellous bone to weight-bearing stress. It may be that when this adaptive function is studied further and understood, replacement elements for parts of long bones destroyed by tumor, infection, or trauma can be used with greater confidence of success. A further study along these lines would give a much sounder basis for the clinical use of replacements than do the occasional clinical attempts adventured upon. In the long run,

there would be much less danger of the method coming into early disrepute because of ill considered or faulty application and its more extended use and wider understanding less delayed. Such instances of a method unjustifiably being thrown into discard because of early faulty application are not difficult to find in medical history. The early odium surrounding open reduction of fractures and internal fixation is only one example.

SUMMARY

A preliminary report on a study in articular replacement is given. Some of the adaptive capacity of cancellous bone to weight-bearing and other stress is considered. Further study along this line is indicated.

REFERENCES

1 Smith-Peterson, M. N.: Arthroplasty of the Hip. J. Bone & Joint Surg., **21**, 269, April, 1939.

2 Harmon, P. H.: Arthroplasty of the Hip for Osteoarthritis Utilizing Foreign-body Cups of Plastic. Surg., Gynec. & Obst., **76**, 347, 1943.

3 Venable, C. S., and Stuck, W. G.: Electrolysis Controlling Factor in the Use of Metals in Treating Fractures. J. A. M. A., **111**, No. 15, 1349, October, 1938.

4 Hudack, Stephen S.: High Chromium, Low Nickel Steel in the Operative Fixation of Fractures. Arch. Surg., **40**, 867, May, 1940.

5 Wise, R.: Histological Study of Transcervical Fracture of Femur After Internal Fixation. J. Bone & Joint Surg., **23**, 941, October, 1941.

AN APPROACH TO RESECTIONS OF THE ESOPHAGUS AND GASTRIC CARDIA

GEORGE H. HUMPHREYS II, M.D.
NEW YORK, N. Y.

SINCE malignant neoplasm of the esophagus and the cardiac end of the stomach are often histologically well-differentiated, and tend to remain localized for long periods before metastasis occurs, it might be expected that they would form a favorable group for surgical cure. At the present time, on the contrary, this group is treated with less success than any other gastro-intestinal cancer. There can be no doubt that one large factor in this lack of success is the frequent absence of arresting symptoms of disease until the lesions are far advanced, but it is also true that the possibilities of adequate treatment are still being worked out, and are not yet generally appreciated.

The isolated success of Torek over 30 years ago, proved that these tumors were not all hopeless, and during the following quarter century his technic was usually resorted to by those surgeons courageous enough to attempt it. The number of successes which were so achieved was very small. Furthermore, if the tumor was found to have crossed the diaphragm into the abdominal esophagus or stomach, or if it proved to be a tumor of gastric origin involving the esophagus by upward extension, this method could not be used, and the situation had to be considered hopeless. Even in those rare cases where removal proved successful, the patient was left with the necessity of submitting to further plastic operative procedures or of resorting to clumsy mechanical devices if he hoped to recover any semblance of eating his food. This operation has, for these reasons, never been a really satisfactory one, and the search for a better solution has been unremitting.

Within the past ten years improvements in our ability to maintain respiration under anesthesia during prolonged intrathoracic procedures, combined with a better appreciation of the rôle of nutritional and fluid needs before operation and during the recovery period, have enabled great advances to be made. Outstanding among these has been the demonstration that direct anastomosis between the stomach and proximal esophagus could be achieved, and that the diaphragm could be crossed without fear. It has also been shown that anastomosis between jejunum and esophagus, either in the abdomen or in the chest, is feasible. While several surgeons have published impressive series of successful resections, and many others have reported isolated or small groups of cases, it is evident that each surgeon has developed his own variations in applying established principles to his particular problems, and that no single generally accepted method has emerged. It seems worth while for this reason to publish the small series here reported.

A total of 70 patients with proven malignancy involving the esophagus were operated upon at the Presbyterian Hospital in the five-year period between

January 1, 1941 and January 1, 1946. In 51 patients the tumor originated in the esophagus; it involved the esophagus secondarily by extension upward from the stomach in 19 patients. An additional group of five patients is included in which the esophagus was not involved, but in which lesions of the stomach close to the cardia were resected through the same approach used in those cases which had extended to the esophagus. Thirty-seven patients, or 52 per cent of the group involving the esophagus, were considered inoperable. Of these, 19 patients were treated by palliative gastrostomy only because the lesion was too far advanced to consider resection; all of these were lesions originating in the esophagus. An operation to determine resectability was carried out in the remaining 18 patients; in 11 of these the lesion originated in the esophagus and the approach was through the chest; in seven the lesion originated in the stomach, and in six of these it was possible to determine operability without opening the chest.

Radical resection of the tumor was carried out on 33 patients, or 48 per cent of the group involving the esophagus. The tumor originated in the esophagus in 21 of these; in the remaining 12 it originated in the stomach. Discussion of the procedures used in these cases, as well as in the five high gastric lesions in which the esophagus was not involved must be subdivided according to the site of the lesion, since this factor determined the method used.

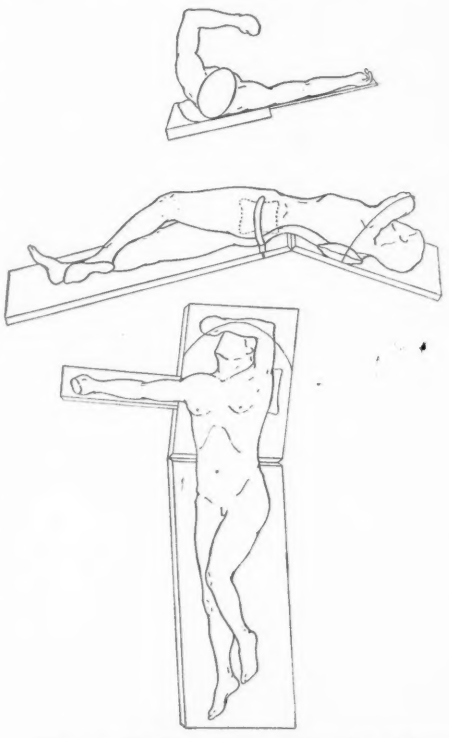


FIG. 1.—Position of the patient for abdominothoracic incision. The table is tilted during abdominal exploration; if the tumor is removable it is rotated back to horizontal, so that the lateral chest wall is exposed. During closure the head and feet are raised to bring the wound edges together.

TUMORS OF THE UPPER THORACIC ESOPHAGUS

The upper level of resection was at or above the inferior surface of the aortic arch in ten patients. Five of these were resected by a procedure of the Torek-type, a right-sided approach being used in all but one. This approach enables the tumor to be exposed readily by dividing the overlying azygos vein, but if the adventitia of the aorta is involved, this fact (which renders resection impossible) may not be uncovered until after considerable dissection has been done. In this series only one patient survived the immediate postoperative period, an operative mortality of 80 per cent, which is considerably higher

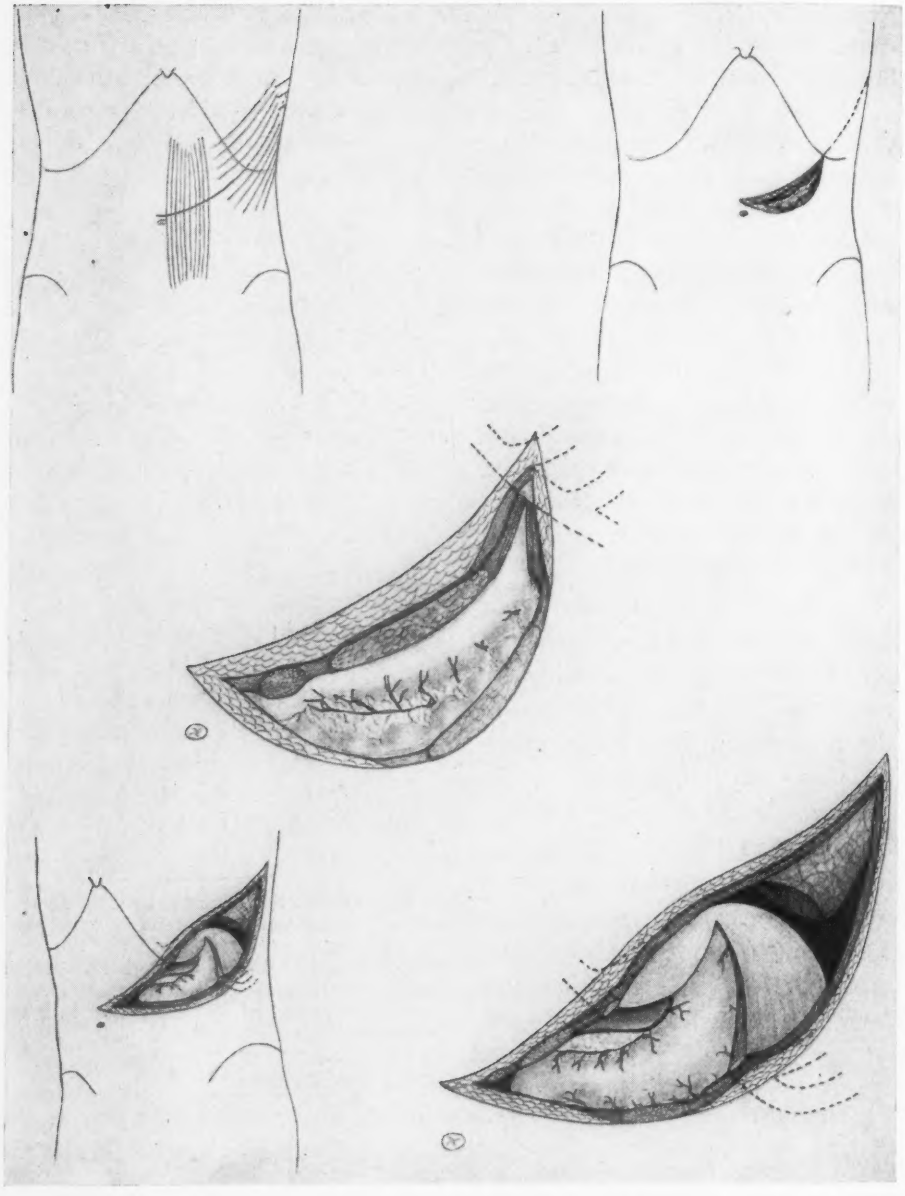


FIG. 2.—The operative incision in the abdominothoracic approach. The abdominal portion is first made and exploration carried out; if the tumor is removable the table is turned and the incision carried up over the 8th interspace. The diaphragm is then divided.

than in any other group. Because of these facts the Torek procedure is now considered to be indicated only when the tumor extends into the cervical esophagus.

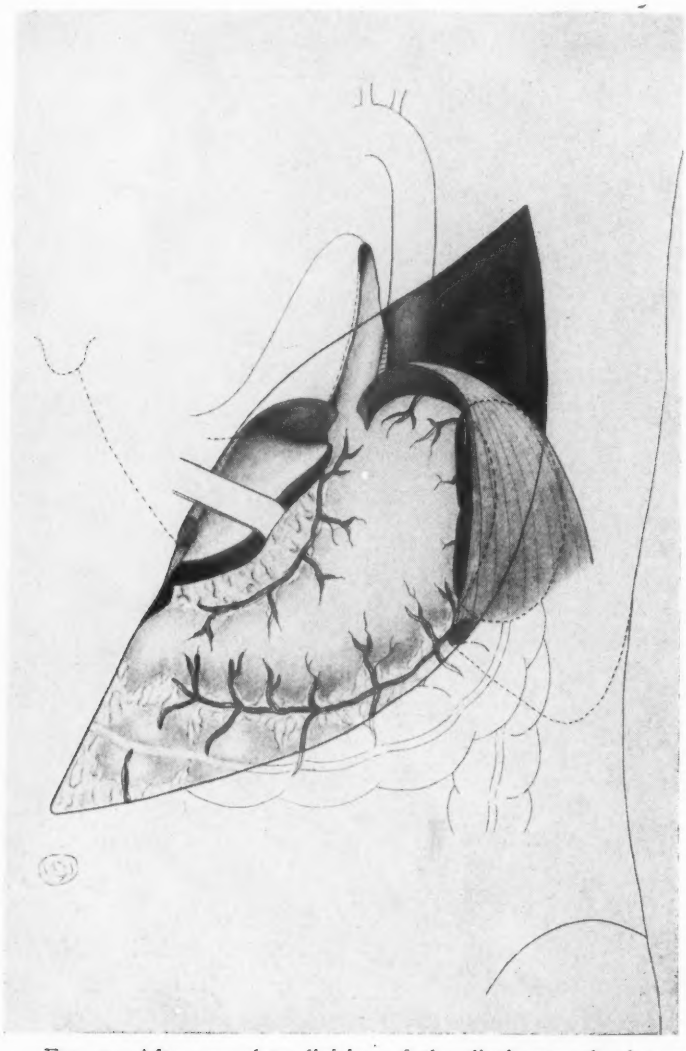


FIG. 3.—After complete division of the diaphragm the lower esophagus and upper stomach is clearly exposed. Exposure can readily be carried upward as high as the lung hilus, less readily to the aortic arch. The pylorus is readily accessible.

A left-sided approach, through a posterolateral incision with division of one or more ribs posteriorly, and either resection of a rib segment or incision through an intercostal space followed by wide resection of the esophagus from well above the lesion to the gastric cardia, and esophagogastrostomy lateral to the aortic arch, is now considered the procedure of choice for these lesions.

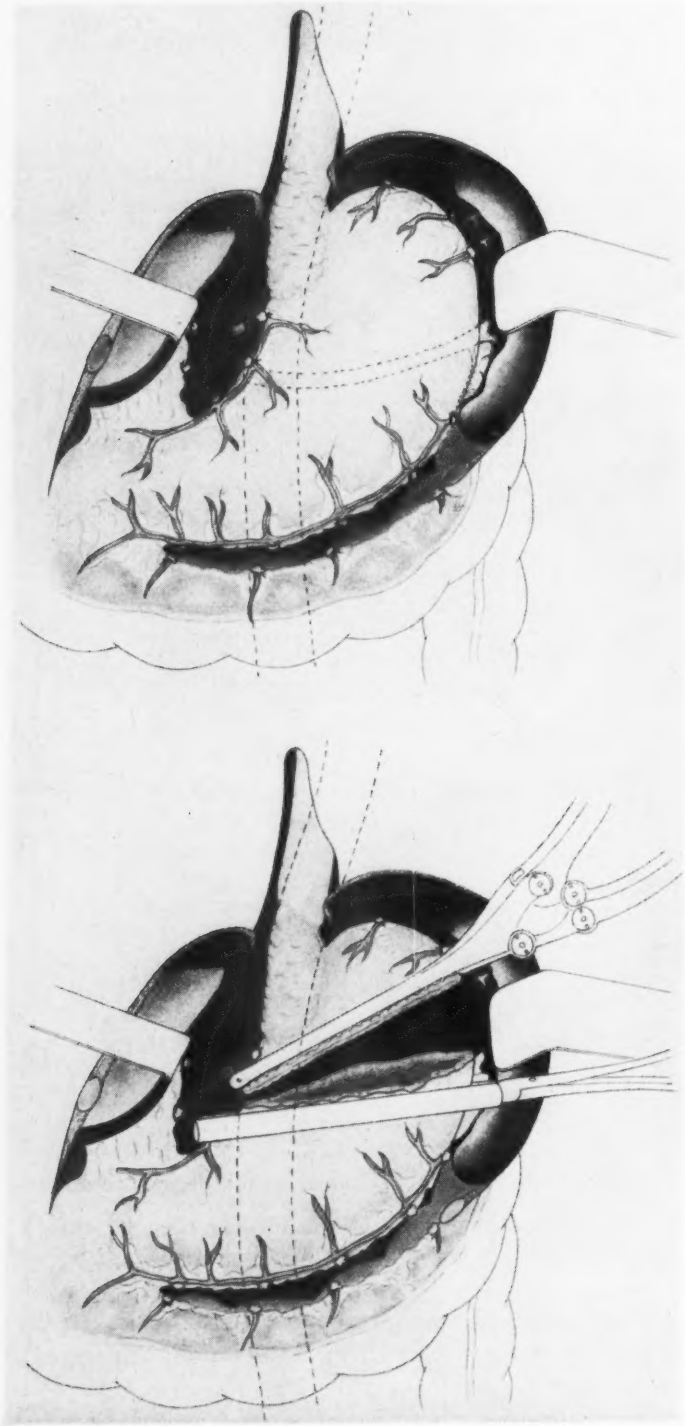


FIG. 4.—Resection of a tumor of the cardia through a combined incision. The gastrocolic and gastrohepatic omenta have been divided (above) and the stomach is being transected (below).

It was carried out in five patients. Operability can usually be determined quickly: if inoperable the thorax is closed and an immediate gastrostomy may be established. If the tumor can be removed, the right pleural cavity will often be entered since the mediastinal pleura on that side is frequently closely

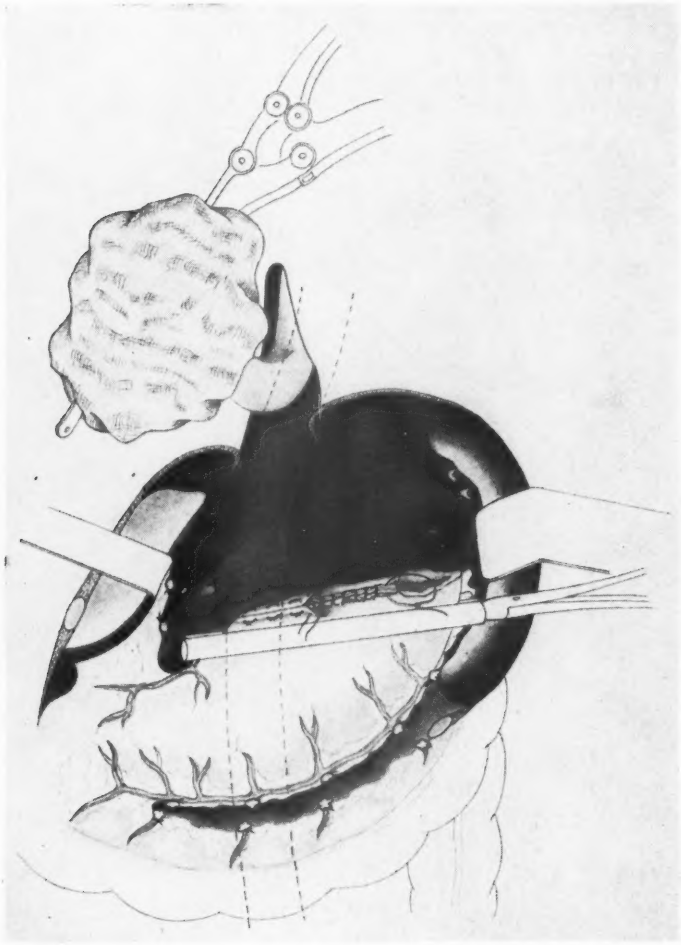


FIG. 5-A

FIG. 5.—Esophagogastrostomy following resection of a tumor of the gastric cardia through a combined incision. The technic is essentially the same when the gastric fundus is used following resection of an esophageal tumor.

(A) The tumor is turned upward and the cut-end of the stomach is closed in two layers.

adherent to the tumor. The esophagus must be freed down to the diaphragm and up to the apex of the chest. The diaphragm is then opened from its dome to the esophageal hiatus and the stomach mobilized by dividing the gastrolienal and gastrocolic omenta, as well as the gastrohepatic omentum including the left gastric artery, until the fundus can be rotated without tension well above the lesion. The esophagus is now divided at the cardia and drawn up behind

the aortic arch to emerge above it between the carotid and subclavian arteries. The cardiac orifice is closed, and the gastric fundus is lifted upward into the chest and secured with its apex lateral to and above the aortic arch, while the body of the stomach lies in the mediastinum in a position corresponding to esophagus. It is surprising how readily the stomach can be brought up—mobilization of the duodenum has not been necessary in any instance. The

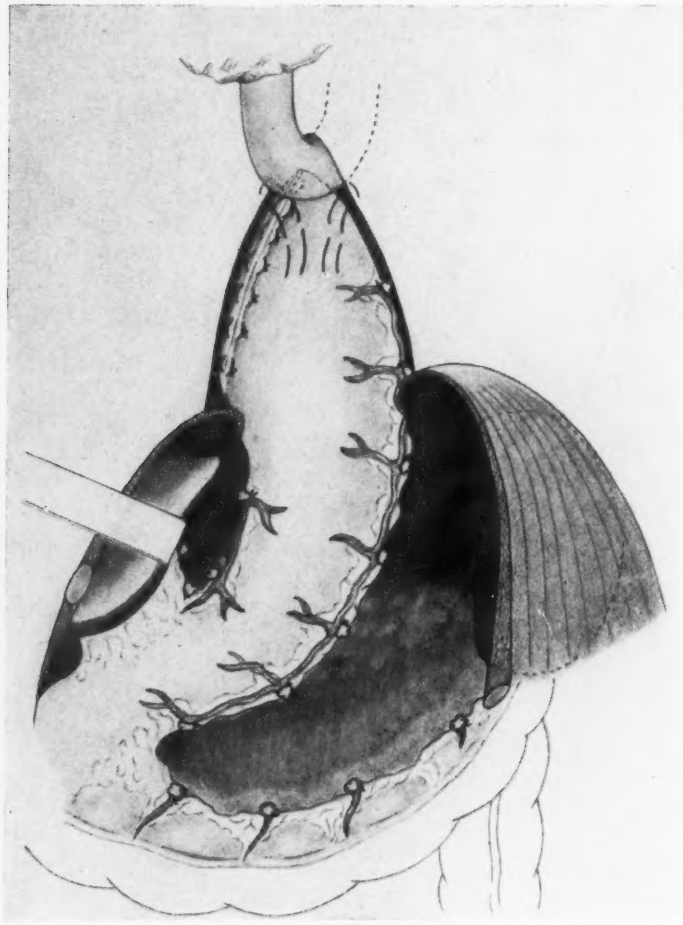


FIG. 5-B

FIG. 5.—(B) The remainder of the stomach rotated upward and anchored in the mediastinum.

esophagus is now divided and its cut-end anastomosed to a vertical incision in the fundus of the stomach, as illustrated in Figure 5. The diaphragm is closed around the stomach and the chest closed with an intercostal catheter drain.

Two of the five patients subjected to this procedure survived, an operative mortality of 60 per cent. One of these died of metastatic tumor two years later, the other is apparently well two years after operation.

The upper level of resection was below the level of the aortic arch in 11 patients. In nine of these resection was carried out through a thoracic approach similar to that used for the higher lesions with esophagogastrostomy below the arch. The level of incision is determined by the expected level of the lesion,

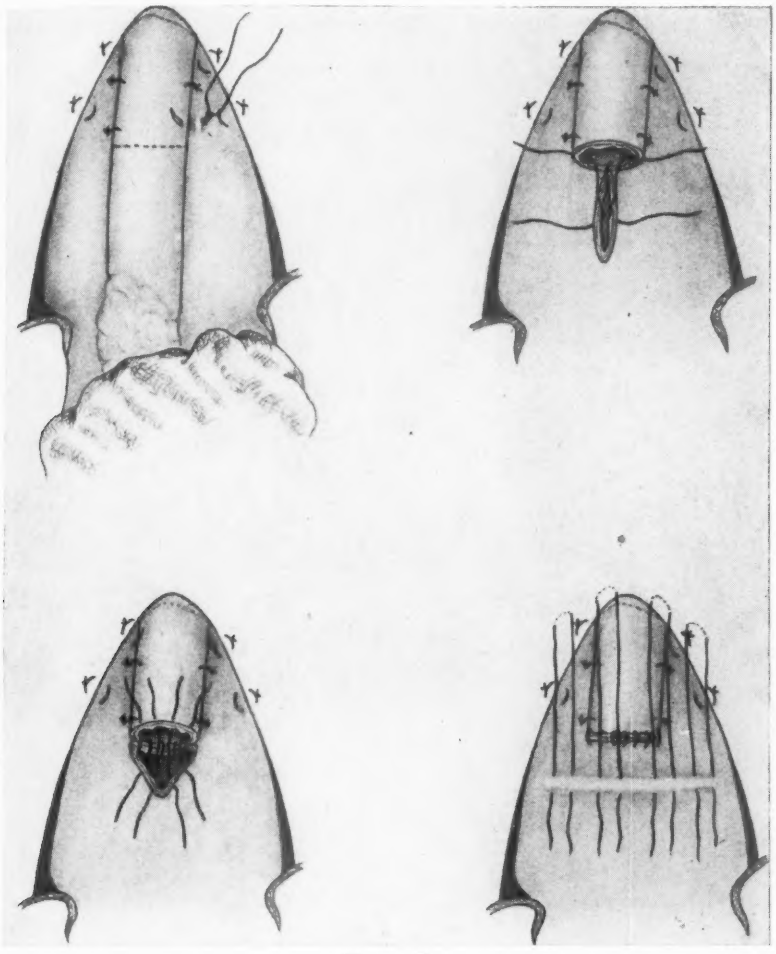


FIG. 5-C

FIG. 5.—(C) Steps in the anastomosis: The esophagus is first sutured to the stomach; after removing the involved esophagus, a vertical incision is made in the gastric wall; interrupted sutures through all layers unite esophagus to stomach; mattress sutures are used to draw the anterior gastric wall upward over the anastomosis and anchor it to overlying pleura.

with extension upward by dividing the necks of the overlying ribs always possible if the upper level of safe resection proves to be too high to permit anastomosis below the arch. In two patients the level was so low that the combined abdominothoracic incision described below was used, in order to determine operability by exploring the abdomen before entering the chest. In all

cases the esophagus is freed from aortic arch to cardia and the diaphragm is divided so as to permit mobilization of the gastric fundus and cardia. Depending on the level of the lesion, it may or may not be necessary to divide the left gastric artery, but mobilization never has to be as extensive as in the higher or lower level groups. The cardiac orifice of the stomach is closed and the fundus rotated upward into the mediastinum where it is held by sutures to the cut edges of the pulmonary ligament. The esophagus is then divided and its cut-

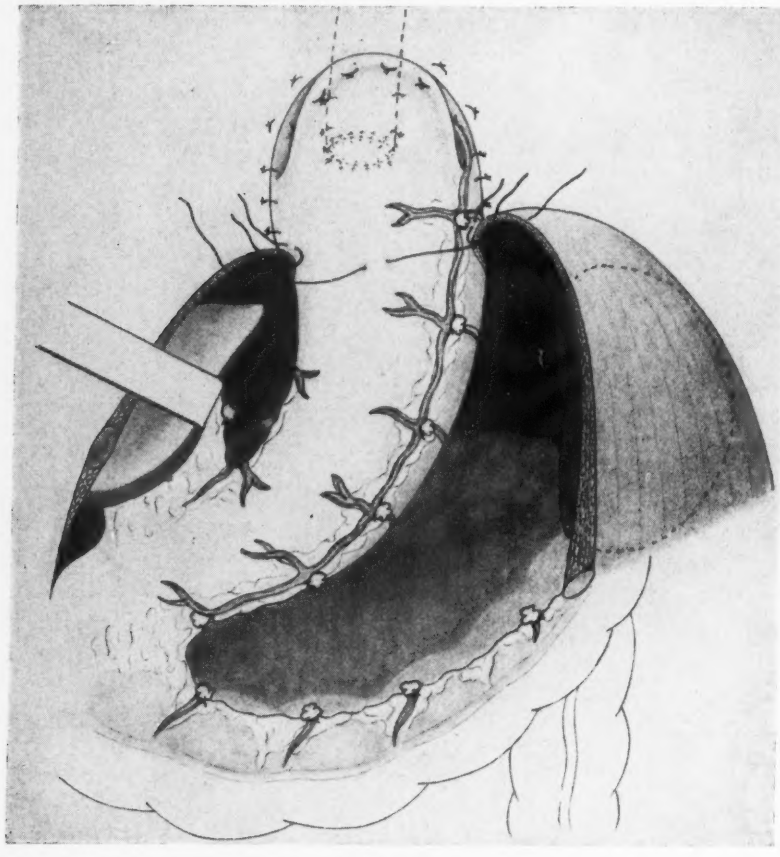


FIG. 5-D

FIG. 5.—(D) The anastomosis completed.

end anastomosed to a vertical incision in the fundus of the stomach, as illustrated in Figure 5. The diaphragm is closed and the chest drained with an intercostal catheter.

Of these 11 patients, five died between three and 19 days after operation, an operative mortality of 45 per cent. One survivor died six months after operation of inanition, though apparently free of malignant disease. Three others succumbed to metastatic recurrence a year, or more, after operation, and the remaining two are apparently well eight and six months after operation.

TUMORS OF THE STOMACH INVADING THE ESOPHAGUS

In ten of 12 patients the tumor, which involved the esophagus secondarily by invasion upward from the stomach, was resected through the combined abdominothoracic approach, as shown in Figures 1 and 2. In the other two a thoracic approach was used, as in the lower esophageal lesions described above. Because many of these tumors are inoperable due to extensive invasion or distant metastases within the abdomen, the latter is first opened through an oblique incision extending from the costal margin at the level of the eighth interspace to a point just to the right of the midline, about two cm. above the umbilicus. If resection is not considered justified (as was the case in the six patients mentioned previously) a palliative gastrostomy may be established, and the patient is spared the added risk of a thoracic operation. If the tumor seems removable the incision is extended directly upward into the chest over the 8th interspace to the posterior axillary line. One or more ribs may have to be divided, though adequate exposure is usually obtained without rib resection. The diaphragm is then divided from its origin at the costal margin between 8th and 9th ribs to the esophageal hiatus. By tilting and breaking the operating table a very wide exposure of the subphrenic region can thus be obtained (Fig. 3). The esophagus is now freed upward as far as is necessary to obtain a good stump for anastomosis, and the stomach, including great omentum and, if necessary, the spleen, is freed from its attachments to liver and colon as far toward the pylorus as necessary. Special care should be taken to remove the group of lymph nodes around the celiac axis when the left gastric artery is divided.

The extent of gastric resection will depend on the extent of the lesion, but it seems probable that in this series there has been a tendency to try to save too much stomach. The procedure, as illustrated in Figures 4 and 5, in which the cut-end of the stomach is closed and brought upward into the mediastinum and a separate anastomosis is made between the cut-end of the esophagus and an incision in the anterior gastric wall, is considered ideal. It is possible, however, only when the lesion is small and close to the cardia. This was the case in only two of the 11 patients in this series. In nine patients the anastomosis was performed instead between the esophagus and the cut-end of the stomach, six times at the greater curvature end, and three times at the lesser. Five of these patients survived for sufficient periods to demonstrate that such an anastomosis can heal and function well, though it is generally condemned by most authors. Probably the greatest risk in such a procedure is the tendency to cut the stomach obliquely, in lesions which extend downward along the lesser curvature, in an effort to save a portion of uninvolved fundus. This results in a long tube-like gastric remnant with questionable blood supply, into the end of which the esophagus is invaginated with difficulty. The only death due to sloughing of the mobilized stomach occurred in such a case.

In the remaining case a total gastrectomy and intrathoracic esophagojejunostomy was carried out. This patient had a very extensive lesion and died during the postoperative period, but it is now felt that this procedure should

be used in most cases in which more than half of the lesser curvature is involved. This opinion is based not only on the theoretic disadvantages of anastomoses between esophagus and the cut-end of a small gastric remnant, but also on experience with some survivors who have developed difficulties due to spasm of the pylorus.

Six of the 12 patients in this group died postoperatively, an operative mortality of 50 per cent. Of the survivors, three have died of generalized metastases, 7, 16 and 18 months after operation. The remaining three are living and apparently free of disease 5, 6 and 15 months after operation.

HIGH GASTRIC TUMORS NOT INVOLVING ESOPHAGUS

Five patients were operated upon using the approach described above because their lesions were so high that it was thought a combined approach might be needed. In two, the procedure was carried out entirely within the abdomen. One of these patients proved to have a leiomyoma of the stomach which was locally removed; the other patient had an extensive carcinoma which, however, did not involve the abdominal esophagus. A subtotal gastrec-

TABLE I

Procedure	Right Posterior Thoracic	Left Posterior Thoracic	Anterolateral Thoraco-abdominal	Abdominal Segment Only	Abdominal Without Exploration	Total Number of Cases	Operative Mortality (Per Cent)
Torek	4	1				5	80
Anastomosis above arch		5				5	60
Anastomosis below arch		9	2			11	45
Esophagogastrectomy and anastomosis		2	10			12	50
Total gastrectomy and gastrojejunostomy (intra-abdominal)			1			1	0
Partial gastrectomy and subphrenic esophago-gastrostomy			1	1		2	0
Partial gastrectomy and gastrorrhaphy			1	1		2	0
Palliative gastrostomy	1	10	1	6	19	37	18
Total	5	27	16	8	19	75	

tomy with subphrenic esophagogastrostomy was performed. In the other three patients a combined abdominothoracic incision was made, but the thoracic esophagus was not disturbed. One of these patients had a large leiomyosarcoma of the fundus resected locally. The second had a partial gastrectomy for carcinoma with subphrenic esophagogastrostomy and the third a total gastrectomy for carcinoma with subphrenic esophagojejunostomy.

It now seems probable that the three patients in this group with carcinoma, two of whom are dead, and one dying of metastases, would have had a better chance of cure if the more radical combined abdominothoracic resection, with anastomosis in the thorax had been done. There was, however, no immediate postoperative mortality in this group. The two patients with leiomyoma and leiomyosarcoma locally removed are living and well, 2 and 2.5 years after operation.

SUMMARY

The various methods of resection of tumors of the esophagus and gastric cardia have been discussed. The experience with 75 patients treated at the Presbyterian Hospital, in New York, during the five-year period from January 1, 1941 to January 1, 1946, has been reviewed, with special reference to the various approaches to the lesions. The procedures carried out and their results are as follows:

1. Esophagectomy with cervical esophagostomy and gastrostomy (the Torek procedure). This procedure, through a right-sided thoracotomy incision is now considered perhaps justified only in lesions involving the lower cervical esophagus. Five cases, 80 per cent operative mortality, no cure.

2. Esophagectomy with esophagogastrostomy lateral to the aortic arch carried out through a left-sided posterior thoracic incision. Five cases, 60 per cent operative mortality, one patient well two years.

3. Esophagectomy with esophagogastrostomy below the aortic arch: nine cases carried out through posterior thoracic incisions, two through an anterolateral combined abdominothoracic incision. Eleven cases, 45 per cent operative mortality, two patients well eight and six months.

4. Esophagogastrectomy with intrathoracic esophagogastrostomy or esophagojejunostomy; two cases carried out through posterior thoracic incisions, ten cases through an anterolateral combined abdominothoracic incision. Twelve cases, 50 per cent operative mortality, three patients well five to 15 months.

5. Partial or complete gastrectomy with intra-abdominal esophagogastrostomy, esophagojejunostomy or gastrorrhaphy: three cases carried out through a combined abdominothoracic incision, two through the abdominal portion only. Five cases, no operative mortality, two patients well 2 and 2.5 years.

6. Palliative gastrostomy: 19 carried out without exploration, 11 after determination of inoperability by thoracotomy, seven after determination of inoperability by the abdominal portion of a combined incision. Thirty-seven cases, 8 per cent operative mortality, longest survival 20 months.

REFERENCES

Clark, D. E.: Transthoracic Esophagogastrostomy for Carcinoma of the Middle Third of the Esophagus. ANNALS OF SURGERY, **121**, 65, 1945.

Carter, B. N.: Resection of a Portion of the Thoracic Esophagus for Carcinoma: Report of Two Cases. Surg. Gynec. & Obst., **70**, 624, 1940.

Churchill, E. D.: Esophageal Surgery. Surg. Gynec. & Obst., **60**, 417, 1935.

Churchill, E. D., and Sweet, R. H.: Transthoracic Resection of Tumors of the Stomach and Esophagus ANNALS OF SURGERY, **115**, 897 and **116**, 566, 1942.

Decker, H. R.: Report of a Case of Esophagogastrostomy for Carcinoma of the Esophagus. J. Thoracic Surg., **5**, 143, 1935.

Eggers, C.: Treatment of Carcinoma of the Esophagus. Surg. Gynec. & Obst., **63**, 54, 1936.

Garlock, J. H.: The Surgical Treatment of Carcinoma of the Esophagus. Surg. Gynec. & Obst., **70**, 556, 1940.

Idem: Surgery of the Esophagus: Section VI, Operative Surgery, edited by F. N. Bancroft, New York, D. Appleton Century Co., 1941.

Idem: The Reëstablishment of Esophagogastric Continuity Following Resection of the Esophagus for Carcinoma of the Middle Third. Surg. Gynec. & Obst., **73,** 23, 1944.

Sweet, R. H.: Transthoracic Resection of the Esophagus and Stomach for Carcinoma. ANNALS OF SURGERY, **121,** 272, 1945.

Torek, F.: The First Successful Case of Resection of the Thoracic Esophagus. Surg., Gynec. & Obst., **16,** 614, 1913.

Yudin, S. S.: The Surgical Construction of 80 Cases of Artificial Esophagus. Surg. Gynec. & Obst., **78,** 561, 1944.

A REPORT ON TRENCH FOOT AND COLD INJURIES IN THE EUROPEAN THEATER OF OPERATIONS
1944-1945

MAJOR OCTA C. LEIGH, M.C.
NEW YORK, N. Y.

A TRENCH FOOT STUDY PROJECT was initiated at the 108th General (U.S.) Hospital, November 15, 1944, by the Chief Surgeon, E.T.O., under the supervision of the Chief Consultant in Surgery and Staff of the 108th General Hospital which was augmented for the endeavor. The purpose of the investigation was to study the pathologic and physiologic changes occurring in such injury and to establish simple methods of rapid *triage* of the patients. During the following three months approximately 500 cases were carefully examined by the group and over 5,000 cases were admitted to the hospital.

"Trench foot" is a diagnostic term used by the U. S. Army Medical Corps to describe the cold injury resulting from prolonged exposure to just-above-freezing-temperature (34° to 40° F.). It has occurred almost exclusively in combat infantry riflemen who were forced into immobility by enemy action. "Frost-bite" is the term used to describe the cold injury resulting from exposure to below-freezing-temperatures—either "ground type" occurring in the ground forces, or "high altitude type" occurring in combat air crews. "Immersion foot" designates the cold injury resulting from prolonged exposure of the feet to cold water. For administrative reasons, these injuries are described as different clinical entities, but it now appears that they all produce similar pathologic changes and can be treated identically. The U. S. Army Medical Corps continues to use the multiple diagnostic terms as they portray a graphic picture of the conditions existing when the injuries were sustained.

During World War I, the French Army reported trench foot as accounting for 3.02 per cent of their battle casualties. During the Italian campaign of 1943 the incidence in the French forces increased to around 10 per cent. Until October 1, 1944, the incidence with the French troops was again around three per cent, which is comparable to the figures in our Army during this period. Following the early November offensive, and again after the German counter-offensive in December, 1944, the U. S. Army casualties increased at an alarming rate, several weeks reaching 50 per cent of battle casualties. During the freezing temperatures of January and February, 1945, a third increase in casualties occurred. This group was classified as cold injuries, ground type, but in this report the two injuries are not separated in the statistical reports. The minor difference in the clinical picture of the injuries will be described later.

In the British Forces operating in Holland and Belgium up to December 31, 1945, only 44 cases of trench foot had been reported. At a joint meeting with the British Medical Consultants in December, 1944, the fact was stressed

TABLE I

TOTAL MONTHLY ADMISSIONS TO HOSPITALS ON CONTINENT

(*Europe Only*)

Date	Battle Casualty	Cold Injuries (Trench Foot—Frost-bite)
Nov. 1944	41,793	6,869
Dec. 1944	37,336	11,469
Jan. 1945	40,107	17,457
Feb. 1945	26,834	7,740
Mar. 1945	31,156	2,151
Apr. 1945	29,997	461

that the British shoe is so constructed and fitted that the front flaps approximate each other before lacing and, therefore, cannot become constricting. Second, in the British Army foot discipline is greatly emphasized and definitely made the joint responsibility of the soldier and his commanding officer. The soldier is repeatedly told that cold is just as dangerous as enemy weapons. Third, during the commitment of troops under conditions resulting in "trench foot," there is a strict rotation policy which relieves the troops before a major injury can occur.

ETIOLOGIC FACTORS IN THE 1944-45 E.T.O. THEATER

In trench foot, the sequence of events leading to the injury followed a fairly constant pattern. The combat infantry soldier is forced into immobility in a wet foxhole for a prolonged period of time. During this period, he first notices tingling or complains of a stinging sensation in his feet, which may become quite intense. After a period of exposure, the feet become numb and finally anesthetic, "like blocks of ice." When the attack is ordered, or he is relieved, walking causes severe burning pain; and on the removal of his shoes, the feet become swollen and warm. Three factors were always present in the carefully examined cases. First, wet cold; second, a prolonged exposure in a relatively immobile position; and third, physical activity following the exposure. Of these factors, wet cold is undoubtedly the most important. Peak casualties always followed periods of wet cold weather.

The secondary etiologic factors which combine with wet cold to produce the final injury are important since they are often correctable (Table II). *Combat activity* was always followed by an increase in trench foot casualties. *Fifty per cent* of the soldiers were injured in their first combat experience. *Proper* and *adequate* foot gear was unavailable in 80 per cent of the casualties during the November, 1944, offensive. After the U. S. Army overshoe was issued, this foot gear proved inadequate in many instances. The important fact that a boot should be designed for rapid removal is not considered in the standard American and British foot gear. Soldiers repeatedly use this excuse for their failure to replace wet socks under combat conditions.

Constriction of the foot and ankle by improperly fitted shoes was difficult to evaluate. Many soldiers complained that their "shoes felt too small after several days of exposure" but the first sign of cold injury is edema and probably caused this complaint.

Prolonged dependency and immobility of the feet appeared important in a few cases occurring in tank crews and artillery squads. These soldiers alone had either dry feet (tank crews) or were in a position to maintain an adequate rotation policy. This suggests that dependency and immobility increase the susceptibility of the feet to cold injury. The soldiers with a history of *previous foot trouble,* either cold injury or other conditions, sustained milder injuries than the entire group examined. Only 20 per cent suffered second- or third-degree injuries as compared to 63 per cent with similar injuries for the entire group. In other words, previous foot trouble made the soldier "foot conscious" and medical aid was requested early.

TABLE II

HEADQUARTERS 108TH (U.S.) GENERAL HOSPITAL, APO 887

ETIOLOGIC FACTORS IN TRENCH FOOT AND COLD INJURIES IN THE E.T.O. 1944–45

Date	Nov. 20 1944	Dec. 21 1944	Dec. 28 1944	Jan. 20 1945	Feb 28 1945
Number Cases Examined	100	100	100	100	100
Type of Troops Affected:	Per Cent	Per Cent	Per Cent	Per Cent	Per Cent
Combat Troops out of Front Lines	98	98	99	100	83
Infantry		76	80	49	74
Armored infantry		18	15	29	7
Paratroop infantry				6	
Airborne infantry			2	4	
	—	—	—	—	—
Total infantry		94	95	88	81
Tanks		5		3	
Field artillery		1	2	5	2
Casuals in reinforcement depots			2	4	17
Total Combat Experience:					
0 to 9 days		50	42	40	51
10 to 19 days		31	23	33	15
20 to 29 days		17	21	7	9
Over 30 days		2	14	20	25
Living Conditions while in Combat					
In foxholes	76	76	89	82	81
In dugouts	8	1	1	3	
In unheated billets	6	5	2	3	4
In tanks or half-tracks	6	6	2	6	
On open ground		5	1	3	
Others	4	7	5	3	15
Supply of Foot Gear in Combat Zone					
Socks (3 or more pairs)	96	46	42	58	90
Arctics, Overshoes or Shoe Pacs:					
None issued	52	38	36	17	10
Issued only after cold injury	28	10	4	5	
Discarded before combat	2	12	15	15	2
	—	—	—	—	—
Total combat troops without protective foot gear	82	60	55	36	12
Issued but inadequate:					
Wading canals or rivers	9	23	9	4	8
Canvas type overshoe leaking	4	10	15	13	16
Rain or snow over tops	3	15	8	15	4
Shoe pac caused excess sweating			2	4	43
Noncombat troops without arctics			2	4	17
History of Previous Foot Trouble:					
Previous cold injury	6	14	17	17	22
Hyperhidrosis	26	30	34	17	7
Other foot disorders previously	10	13	13	5	9

The most important *correctible secondary factor* is an improved rotation policy for troops during combat activity. If a few men are relieved for only an hour daily from each group, adequate foot care could be required under supervision, if necessary. This was almost impossible when the tactical situation required troops to wade streams and "dig in" until relief arrived. Company commanders most successful in avoiding casualties under these circumstances, required each soldier to exchange old wet socks for clean dry ones when daily food rations were issued. This often required the mess sergeant to deliver food and clean socks from foxhole to foxhole during the hours of darkness.

REACTION OF THE SKIN TO COLD

Lewis,[1] Stray,[2] and Kreyberg[3] agree that the immediate reaction of the skin to cold is a blanch in color. This phenomenon is caused by the contraction of the terminal arterioles and veins. It is doubtful that the distal capillary loops are involved but the reduced blood flow causes the lumen of these vessels to appear smaller in diameter.

The sensation of cold appears as the skin temperatures are reduced to 25° to 15° C. At these temperatures, the skin develops a bluish color (cyanosis) indicating local oxygen deficiency, *i.e.*, local tissue metabolism exceeds local oxygen supply. As the temperatures are lowered to 10° to 8° C., the bluish color gradually changes to purple and finally a bright red or pink. This paradoxical color change, indicating excess oxygen locally, is apparently the result of decreasing tissue metabolism and a lower oxygen dissociation from the blood at these temperatures.

Each of the above color changes may be transient or prolonged depending upon the degree of cold, duration of exposure and speed of wind currents. If the surrounding temperature is returned to normal after a short exposure, no further reaction will occur. If prolonged, secondary pathologic reactions may follow. The transition between these physiologic responses and pathologic reactions is altogether too indefinite. Spellman[4] has reported minimal blood flow in the legs at temperatures between 20° to 15° C. Prolonged exposure at these temperatures, the "just-above-freezing" encountered by the troops, produces definite pathologic changes.

CLINICAL TYPES IN TRENCH FOOT

In mild or first-degree injuries, (36.4 per cent)* the color changes and sensations encountered during exposure are quite similar to those described above. When placed in a warm environment, the foot develops a bright red flush with a slight elevation of skin temperature. The great vessels show increased pulsation for a few hours and the skin appears thicker from mild edema (Fig. 1). The patients experience "tingling" of the feet early, and later complain of itching, burning or mild throbbing pain. This so-called "hyper-

* Based on 500 cases discharged from 108th General Hospital.

emic" or "inflammatory" stage subsided within three days (1 to 6 days), after which the foot assumed a normal appearance. All cases were walking without pain within 4.2 days (0–10 days) after exposure. This group of cases were returned to full duty after a short period of rehabilitation.

In the second- and third-degree injuries, the color changes are more pronounced during the period of exposure. The moderate cases describe the

FIG. 1.—Trench foot, first-degree, early, showing persistent red flush and edema.

foot as pale with areas of blue and purple discoloration. Severe cases describe the foot as "marble white" in color. Difficulty in walking and anesthesia of the feet increased with duration of exposure.

In the *second-degree injuries,* (55.6 per cent)* the reaction after exposure is more severe, with hyperemia, pulsation of the larger vessels and throbbing pain which may last for several days (Fig. 2). Blisters appear and minute areas of intracutaneous ecchymosis develops on the weight-bearing surface of the foot and toes (Fig. 2B). The edema subsided on the average of 8.4 days (6–10 days) and was followed by varying degrees of scaling, leaving a sensitive skin that perspired profusely. When placed in warm environment or during exercise, the feet become warm and painful. Exposure

* Based on 500 cases discharged from 108th General Hospital.

to a cold or cool environment is more comfortable for the patient. This is in contrast to the recovering cases with high altitude frost-bite whose hands become painful when exposed to cold.

Most of these cases developed a typical foot deformity. The longitudinal and transverse arches would disappear and the great toe contract into a semi-dorsiflexion position. Deep-seated pain continues for weeks usually in the first metatarsal-phalangeal joint and across the plantar surface of the foot, especially when soldiers were given trial marches or required to stand guard of two-hour periods. Under the urgency of the time, most of these cases were returned to limited duty, usually requiring guard duty in the rear echelon. Many were rehospitalized and later discharged as unfit for any type of duty.

In the *third-degree injuries,* (eight per cent)* the initial reaction was intense and usually develops within three to four hours after the foot was placed in a warm environment (Fig. 3A). All the cardinal signs of inflammation are present—marked edema, heat, redness and burning throbbing pain. Large blisters, intracutaneous ecchymosis with superficial skin necrosis give the appearance of threatening gangrene of the foot and digits (Fig. 3B). The inflammatory stage averaged 12.4 days (7–32 days), only rare cases showing persistent edema for more than 14 days. The superficial layers gradually mummified and finally desquamated (Fig. 3C) shedding the shrunken gangrenous shell of epidermis like a cocoon, leaving a pink sensitive skin resembling the foot of a baby (Fig. 3D). On dependency, the skin assumed a dusky, cyanotic color (Fig. 4A and B) in many third-degree injuries. None of these cases could walk without severe pain and disability during the three months period observed. All were evacuated to the U.S.A. as unfit for further duty.

In the casualties with cold injuries, ground type, which appeared during the freezing weather in January-February, 1945, the clinical course was identical except edema and blisters were often localized to areas around the great toe. This, of course, has varied considerably, making it impossible to separate the cases clinically except by a history of freezing temperatures.

One severe cold injury of both feet was trapped for five days behind enemy lines and forced to feign death to avoid capture. During this period, he lived in a snow-filled foxhole where his feet became encased in blocks of ice. After five days, he walked and crawled several miles to friendly lines where his shoes were cut off the frozen feet (Fig. 5). This is the only case that required amputation of feet for gangrene. Digits were lost in only one per cent of the 500 carefully followed cases.

The percentage of first, second and third-degree trench foot and cold injuries, ground type, was approximately identical.

* The material studied consisted of 24 biopsies from cases in various stages of the injury and four amputated toes.

FIG. 2-A.—Trench foot, second-degree, early. Right foot shows blister on great toe.

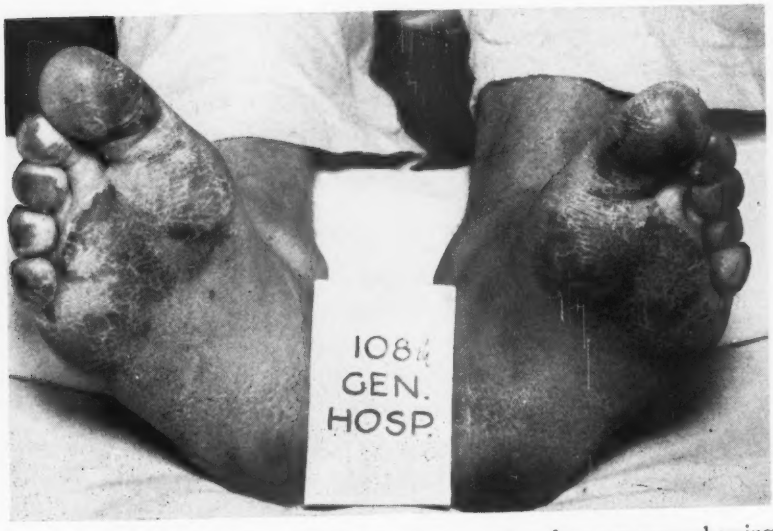


FIG. 2-B.—Trench foot, second-degree, three weeks after exposure showing intracutaneous ecchymosis and early exfoliation.

FIG. 3-A.—Trench foot, third-degree, early, acute inflammatory reaction two days after exposure.
3-B.—Same as 3-A, two weeks after exposure, showing edema receding and early mummification of the superficial layers, suggesting impending gangrene.
3-C.—Same as 3-A, four weeks after exposure, showing desquamation of superficial layers of skin.
3-D.—Same as 3-A, six weeks after exposure, delicate skin beneath the mummified superficial epidermis.

PATHOLOGIC CHANGES IN TRENCH FOOT

In the acute early inflammatory stage, edema, intracutaneous hemorrhage and necrosis was found in the stratum corneum of the skin (Fig. 5). Davis, *et al.*,[5] found the separation of the epidermis from the dermis with a loss of the basal germinal layer in high altitude frost-bite, whereas the basal germinal layer was always intact in the trench foot cases examined (Fig. 6).

Round cell infiltration was present in the perivascular spaces. Suppuration was found only in toes amputated for gross secondary infection. In the late cases (4–6 weeks after exposure) the skin thickness was decreased and sweat glands rare. A proliferation of fibrous tissue was present in the corium and often around nerves. Nerves showed axis cylinder degeneration in early stage and later, evidence of regeneration. The minute vessels showed perivascular round cell infiltration with diapedesis of red blood cells in the severe early cases. Late cases showed thrombosis of terminal arterioles in areas with skin necrosis.

The exact mechanism of the development of skin necrosis after cold injuries is still controversial. Most authors[5, 6, 7] report a true thrombosis of the terminal arterioles and veins, but Kreyberg[3] reports this as a secondary complication. Kreyberg and Rotens[8] have demonstrated patent capillary vessels immediately after experimental freezing. By using a vital dye technic, they showed increasingly capillary permeability through the vessel walls immediately after exposure. As the exposure increased, permeability increased to a degree that all plasma escaped leaving tightly packed blood cells within the lumen of the minute vessels. This "stasis" or "intravascular mass" of blood cells would finally form a mechanical obstruction to blood flow within minutes or hours after the exposure. The area in which stasis develops would later become necrotic. Secondary "true thrombosis" might develop in or about the tissue doomed to necrosis.

This phenomenon has recently been demonstrated by Essex and Quintanilla[10] by direct observation of a peripheral capillary bed after the insertion of transparent chambers in the ears of rabbits. In addition, these authors demonstrated that the stasis was not caused by coagulation since the identical phenomenon was observed in the vessels of animals after their blood had been rendered incoagulable by injections of heparin.

Most clinicians advise slow restoration of blood flow after exposure to cold to avoid stasis and skin necrosis. This viewpoint lacks experimental or clinical confirmation. The recent beneficial results reported by Lange and Boyd[6] in the prevention of skin necrosis by heparinization after freezing may be due to the prevention of secondary true thrombosis developing proximal to the areas of stasis.

EVACUATION AND CARE OF TRENCH FOOT

The Evacuation and Disposition policy of the First Army and Communication Zone Hospitals are shown in Chart I. Soldiers reporting into

Fig. 3-A.—Trench foot, third-degree, early, acute inflammatory reaction two days after exposure.
3-B.—Same as 3-A, two weeks after exposure, showing edema receding and early mummification of the superficial layers, suggesting impending gangrene.
3-C.—Same as 3-A, four weeks after exposure, showing desquamation of superficial layers of skin.
3-D.—Same as 3-A, six weeks after exposure, delicate skin beneath the mummified superficial epidermis.

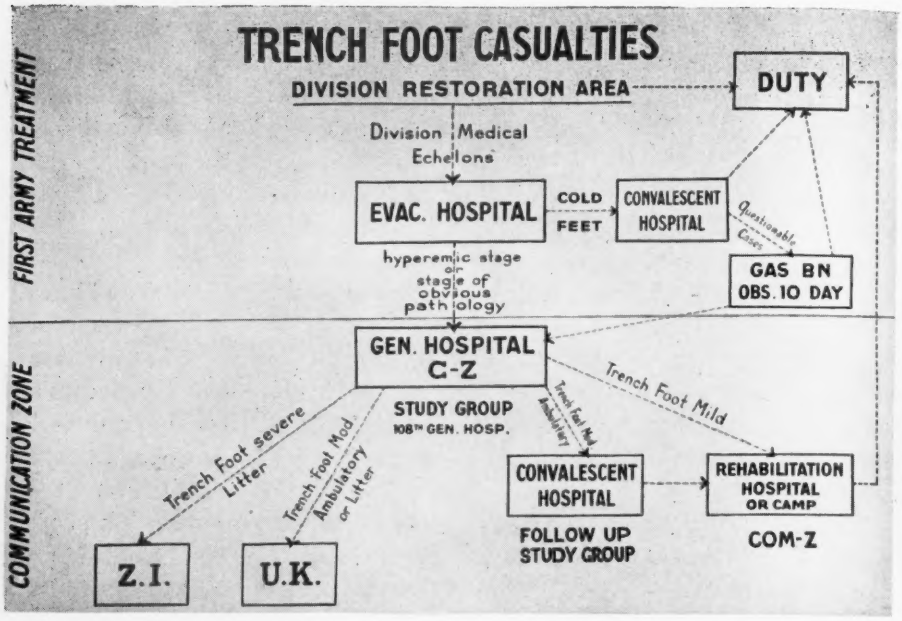


CHART I.—Evacuation and disposition of trench foot casualties E. T. O., 1944–45.

Battalion Aid Stations with "cold feet" should be immediately sent to a nearby "Restoration Area" for at least 24 hours' observation. Experienced clinicians have difficulty in estimating the degree of injury until the reactive hyperemia or inflammatory reaction develops. In the Restoration Area, the *most important point in the evacuation chain,* all "cold feet" should be given a cold foot bath and placed in a cool dry bed. Warm food and drink should be given to restore normal body temperature and gradual, slow restoration of normal blood flow of the feet. External heat, walking or vigorous massage is avoided at this period.

The nurse or doctor should follow the vascular response closely. Simple palpation of the feet at hourly intervals will detect an elevation of skin temperature or a bounding arterial pulse. When these signs of the onset of hyperemia appear, the feet are exposed to a cool environment with the feet elevated on pillows. These measures are favored by clinicians who hold that slow restoration of blood flow will avoid stasis in the capillary bed which subsequently leads to skin necrosis. Pressure bandages over cotton has also been recommended and apparently affords the patient some relief from pain and decreases the edema. After 24 hours of observation, accurate classification of the degree of injury should be accomplished easily. Second- and third-degree injuries are evacuated to General Hospitals where prolonged treatment will be necessary. First-degree injuries, or soldiers escaping without reactions, can be returned to duty after a short rest period. Early accurate diagnosis should avoid the mass evacuation of mild injuries which caused so much

confusion on their arrival at General Hospitals. These cases showed little or no objective evidence of the injury and were often mistaken for malingerers.

Once the hyperemia has developed, the treatment is directed toward preserving the superficial injured layers of epidermis which forms a tough, dry protective covering of the viable layers beneath. The foot is exposed to a cool dry environment, and elevation on pillows continued. The procedure has been likened to the process used in "curing" a ham. The application of

FIG. 4-A FIG. 4-B

FIG. 4-A.—Trench foot, third-degree, two months after exposure. Except for scaling, the feet appear normal.

4-B.—Same as 4-A, showing dusky cyanotic discoloration on dependency. This position causes considerable pain.

ointments, repeated massage or foot baths may produce rents in the protective layer and allow the ingress of secondary infection. The injured layers of epidermis will gradually shed as healing is completed.

Surgical amputation should never be done in the early stages except for gross secondary infection. Toes that appear gangrenous may have much viable epidermis beneath the black outer layers. Dry gangrene of the toes occurred in only one per cent of the carefully followed cases. If infection is present, sulfa drugs and penicillin should be used as in any other infection. Tetanus toxoid was given in cases with obvious open wounds. In the vast majority of cases with trench foot, however, the drugs are not necessary.

After the edema has subsided, the treatment is directed toward the prevention of foot deformities caused by atrophy of muscles and the secondary fibrosis which develops. Much difficulty was encountered in the soldiers who were first treated by prolonged bed rest. The resumption of walking or exercise of the feet is often painful. Gentle massage and supervised passive and active exercise as soon as the edema has subsided will prevent this psychologic block from developing. In the mild cases, this therapy is started immediately. It is

FIG. 5.—Cold injury, ground type, third-degree, one month after exposure, showing gangrene of both feet.

FIG. 6.—Photomicrograph of section from blister in third-degree trench foot. The separation in the epidermis shows the basal germinal layer intact.

important to explain that continued inactivity will produce increasing muscular atrophy, joint stiffness and even permanent disabling contractures of the feet. All first- and second-degree injuries should be offered socks and shoes and encouraged to walk within pain limits at the earliest possible moment. When allowed the privileges of the Post Exchange, movies and American Red Cross, it is surprising how quickly the American soldier will walk without disability.

The use of vasodilator drugs and lumbar sympathetic block was investigated and found to give no relief from pain or decrease the convalescent period in the acute cases under observation.

SUMMARY AND CONCLUSIONS

1. The extent and causes of the American trench foot casualties during the 1944-45 European Campaign have been presented.

2. A classification of clinical types based on the severity of the injury is presented as used to facilitate rapid disposition of casualties.

3. The pathologic and physiologic changes in trench foot are similar to

frost-bite but less severe. The basal germinal layer of epithelium remains intact in trench foot but is lost in frost-bite.

4. The present accepted methods of evacuation and treatment of trench foot is discussed.

630 West 168th St.

REFERENCES

1 Lewis, Thomas: Observations on some Normal and Injurious Effects of Cold upon Skin and Underlying Tissues: Reactions to Cold and Injury of Normal Skin. British Med. J., **2**, 795, 837 and 869, 1941.

2 Stray, Kristian: Experimental Investigations of the Reaction of Skin to Cold. Oslo, 1943.

3 Kreyberg, Leiv: Report to the Commanding Officer, 108th General (U. S.) Hospital on "Some Notes and Considerations Regarding Injuries from Cold." Paris, 1945.

4 Spellman, C. R.: Blood Flow through the Extremities at Low Temperatures and its Possible Relation to Immersion Foot. Report I. Naval Medical Research Institute, Bethesda, Md., January 10, 1944.

5 Davis, Loyal, Scarff, John E., Rogers, Neil, and Dickinson, Meredith: High Altitude Frost-bite. Surg., Gynec. and Obst., **77**, 346, December, 1943.

6 Lange, K., and Boyd, L. J.: Functional Pathology of Experimental Frost-bite and Prevention of Subsequent Gangrene. Surg., Gynec. and Obst., **80**, 346, October, 1945.

7 Ungley, C. C., and Blackwood, W.: Peripheral Vasoneuropathy after Chilling. Lancet, **2**, 447, October, 1942.

8 Kreyberg, L., and Rotnes, P.: Le stase experimental et une method pour le mettre en evidence par preparations speciales. Soc. Biol., **2**, 895, 1931.

9 Essex, H. E., and Quintanilla, R.: Effects of Frost-bite on the Minute Blood Vessels of a Peripheral Vascular Bed. Proceedings of the American Physiological Society, **5**, 25, February, 1946.

WAR-TIME ACTIVITIES OF THE NATIONAL RESEARCH COUNCIL AND THE COMMITTEE ON MEDICAL RESEARCH; WITH PARTICULAR REFERENCE TO TEAM-WORK ON STUDIES OF WOUNDS AND BURNS

JOHN S. LOCKWOOD, M.D.*

NEW HAVEN, CONN.

THE MOBILIZATION of civilian research toward meeting the special problems of military medicine and surgery commenced in the spring of 1940, when the Division of Medical Sciences of the National Research Council was requested by the Surgeons-General of the Army and Navy to assemble advisory committees of specialists to aid them in achieving for their respective services the best modern standards of professional practice.

The Committee on Surgery of the National Research Council held its first meeting on June 15, 1940, under the chairmanship of Dr. Evarts Graham. Within the succeeding months there were organized thirteen subcommittees, on Surgical Infections, Neurosurgery, Plastic and Maxillofacial Surgery, Thoracic Surgery, Anesthesia, Radiology, Orthopedic Surgery, Burns, Ophthalmology, Otolaryngology, Physical Therapy, Urology, and Vascular Injuries. The Subcommittee on Surgical Infections and the Subcommittee on Burns were combined in December, 1943 to form the Subcommittee on Infected Wounds and Burns, under the chairmanship of Dr. Allen O. Whipple.

It is the main purpose of this article to review, in broad outline, the program of research which was conducted under the advice and sponsorship of this Subcommittee, not only for the purpose of acknowledging the leadership and inspiration which was provided by its Chairman, but also in order to present to the readers of this journal an historical account of a unique experiment in coöperative surgical research on a national basis. A much fuller account of the work is to be published in conjunction with the History of the Committee on Medical Research of the O. S. R. D. The scientific record of the individual contributions has in large part been published in the surgical literature of the past four years; this account will, therefore, be concerned only with the general aspects of the program of work on wounds and burns and surgical infections, particularly in regard to the background of organization, and the technic of approach. It is hoped that many readers of this journal who were serving throughout the war as medical officers in overseas theaters, and who were necessarily out of contact with the war-time civilian research program, may be interested in knowing something of the method of organization, the difficulties, and the successes, which attended this effort on the home front.

* Chief, Division of Surgery, Committee on Medical Research of the Office of Scientific Research and Development, Washington, D. C.

GENERAL ORGANIZATION OF CIVILIAN MEDICAL RESEARCH

During the period between May, 1940 and August, 1941 the functions of the Committee on Surgery of the N. R. C. and its subcommittees, were limited largely to rendering advice on specialized problems presented to them by the Surgeons-General. It was recognized that the value of some of this advice was limited by the unfamiliarity of most of the Committee members with the special medical aspects of modern warfare, and by the considerable gaps in knowledge which could only be filled by new research. However, no machinery existed to permit the sending of teams of experts to the war theaters where our prospective allies were engaged, and no funds were then available to support the comprehensive program of research which was thought to be required. The problem of funds was solved, however, when President Roosevelt established, in August, 1941, the Committee on Medical Research as a unit of the Office of Scientific Research and Development, and provided it with substantial funds to be employed in research into all phases of military medicine. The Committee on Medical Research immediately requested the National Research Council to serve in an advisory capacity to aid in determining how these funds could best be employed, and the administrative headquarters of the two agencies were established under the same roof in the National Academy—Research Council building in Washington. The membership of the C. M. R. comprised Dr. A. N. Richards, as chairman, Dr. Lewis H. Weed as vice-chairman (Dr. Weed is also Chairman of the Division of Medical Sciences of the N. R. C.), Rear-Admiral Harold W. Smith, representing the Navy, Brig. Gen. James S. Simmons, representing the Army, Dr. R. E. Dyer, representing the Public Health Service, and Doctors A. B. Hastings and A. R. Dochez. This Committee was authorized to make recommendations to the Director of the O. S. R. D., Dr. Vannevar Bush, concerning the expenditure of federal funds for research on problems in the medical field. The funds were made available to each individual investigator through a contract developed between the O. S. R. D. and the institution with which he was associated.

Since the C. M. R. was responsible not only for the initial allocation of funds, but also for the manner in which these funds were spent, it became necessary, as the program expanded, to develop a scientific administrative organization under six main divisions, in Medicine, Surgery, Chemistry, Physiology, Aviation Medicine, and Malaria Studies. The Chiefs and Deputy Chiefs of these Divisions were specialists in the subjects covered by the several divisions and gave major portions of their time to the work of maintaing contact with the investigators, the advisory committees of the N. R. C., and the staffs of the Surgeons-General. The Division Chiefs represented the government as scientific officers on the contracts in their respective divisions.

An hypothetical case will serve best to illustrate the practical operation of the program in its final stage of evolution. Thus, a request by the Army for advice as to the best method of determining the prognosis of frost-bite injury might be transmitted through the National Research Council to the Subcommittee on Vascular Injuries. The problem would be discussed at a meeting of

the group in Washington, with representatives of the Army and Navy and other invited consultants in attendance. Having decided that further research on the problem was needed, the Subcommittee would suggest one or more individuals who might be qualified and prepared to undertake the work; the Chief of the Division of Surgery of the C. M. R. would then approach these individuals, perhaps visiting them in their laboratories in order to determine the adequacy of facilities and their willingness to undertake the work. An application for funds would then be prepared, including a brief description of the plan of attack; this would be transmitted back to the Division Chief, who would refer it to the Subcommittee on Vascular Injuries and the Committee on Surgery if he felt that further advice was necessary; it would then be submitted to the Committee on Medical Research with the final recommendation of the National Research Council and the Division Chief. After the C. M. R. had approved the proposal, the Director of the O. S. R. D. would authorize the initiation of a contract to cover the expenses of the work, including salaries, materials, and overhead costs. The investigator was expected to submit bimonthly progress reports to the C. M. R., and these would be further distributed to the N. R. C. committees concerned, to other interested investigators, and to the armed Services. The investigator might be requested to come to Washington at intervals to make direct reports on his work in conference with other specialists in the field, and to learn of other related work in progress. Finally, when his work had reached a definitive conclusion, it would be made the subject of a formal recommendation from the N. R. C. to the Surgeons-General; who would then decide whether or not the recommendation should be adopted in military practice, and made the subject of a final recommendation to the Surgeons of the respective Service Commands and Theaters. This procedure was undoubtedly time-consuming and cumbersome; to some extent it was developed through historical evolution rather than deliberate design; however, it usually afforded maximum latitude to the investigator in the planning and conduct of the actual work in the designated subject; it provided a necessary measure of advice and coördination by experienced leaders in the general field; and it satisfied the stringent legal requirements regarding the expenditure of public funds by private institutions. The investigator was expected to adhere to the subject of the contract in the conduct of his work, but the subjects were usually capable of broad definition, and allowed the investigator to employ initiative and originality in his work.

A total of one hundred contracts were developed for work in the surgical field—representing total allocations of almost $3,000,000, some of which was not spent. About one-half of this sum was appropriated for work on the prevention and treatment of infections in wounds and on burns. The remainder was divided almost equally between neurosurgical problems and research in the other surgical specialties.

FUNCTIONS OF THE N.R.C. COMMITTEES

Some of the N. R. C. committees functioned more actively than others, owing to the great variations in the scope of the tasks assigned to them. Between meetings the business of the committees was conducted by correspondence and by telephone. Meetings were held at irregular intervals, depending upon the urgency of matters under consideration, but, in most cases, several times a year. The three main functions served by these committees were:

1. To provide opportunities for informal exchange of experience between men with similar problems and interests from civil life and from the armed Services.

2. To draft formal recommendations upon request of the armed forces or other governmental agencies.

3. To sponsor and review proposals for contract submitted to the Committee on Medical Research.

The Committee on Surgery held sixteen meetings, the Subcommittee on Surgical Infections held twenty-one meetings prior to December, 1943, when it was merged with the Subcommittee on Burns; the latter group met eleven times prior to the merger, and the combined Subcommittee held ten meetings. Dr. Frank L. Meleney was chairman of the original Subcommittee on Surgical Infections and gave unstintingly of his time and energy in leading the work of this group during the period of active investigation of the use of sulfonamides in the prevention of infections in accidental wounds. As stated previously, Doctor Whipple, who had served as Chairman of the Subcommittee on Burns, became chairman of the combined Subcommittee on Infected Wounds and Burns in December, 1943, and continued in this capacity until April, 1945, when he was succeeded by Dr. Fred Coller.

In addition to formal meetings of these committees, there were held many *ad hoc* conferences on special subjects which representatives of the surgical committees were requested to attend; these included conferences on shock, blood transfusions and blood substitutes, effects of war gases, surgical manuals, and new hemostatic agents. These conferences brought together representatives of several specialist groups, including internists, physiologists, and biochemists, as well as surgeons. On numerous occasions surgical representatives travelled to Ottawa to attend meetings of the corresponding committees of the National Research Council of Canada, thus, providing a valuable liaison between these groups.

The minutes of all meetings and conferences were recorded in detail, together with abstracts of the scientific papers presented, and were mimeographed and distributed to those who had attended, and to other interested individuals.

The magnitude of the task confronting the administrative and clerical personnel of the National Research Council is reflected in the fact that between May, 1940 and December, 1945 there were held 653 committee meetings and

223 special conferences, attended by a total of 19,760 individuals. In one year alone, the report section of the Division of Medical Sciences edited, mimeographed, and mailed a total of 262,156 copies of 2,718 reports from O. S. R. D.-C. M. R. investigators which required 11,925 stencils and 662,749 sheets of paper![1] The Records Section of the C. M. R. received all progress reports, interim reports, manuscripts for publication, and final reports, gave the necessary clearance whenever security restrictions were involved and distributed to all investigators and to the medical services of the Army and Navy a weekly bulletin containing abstracts of the reports received. There can be no doubt that the medical research program had its share in contributing to the general shortage of paper! It should also be remarked that those who labored on this aspect of war-time research made a contribution of the greatest importance. Without this editorial and information service the organizations could not have functioned because the usual channels of medical information could not have begun to meet the need for the rapid exchange of information required.

The members and administrative officers of the C. M. R. maintained offices in Washington, giving to government service the first claim upon their time, but in many cases continuing to carry part-time responsibilities in their home institutions. Valuable assistance was rendered by a number of technical aides, who gave up their regular professional work in order to devote full-time to government service.

SUBJECTS OF C.M.R. CONTRACTS IN THE SURGICAL FIELD

The distribution of the O. S. R. D.-C. M. R. contracts exclusively in the surgical field is shown in Table I.

TABLE I

	No. of Contracts
Prevention and Treatment of Surgical Infections	26
(Of these, seventeen were primarily concerned with patients and nine were primarily laboratory investigations)	
Studies on the Pathologic Physiology and Treatment of Burns	19
(Of these, eleven were primarily concerned with patients and eight were primarily laboratory investigations)	
Statistical Analysis of Wound and Burn Studies	1
Orthopedic Problems and Prosthetic Devices	8
Cold Injury (including frost-bite and trench foot)	6
Anesthesia and Pulmonary Physiology	2
Peripheral Nerve Repair	14
Concussion	10
(Of these, six were primarily concerned with patients and four were primarily laboratory studies)	
Absorbable Hemostatic Cellulose	1
Collagen Sutures	2
Wound Ballistics	2
Plastic Surgery	1
Ophthalmology	4
Radiology	2
Vascular Surgery	21
Protein Loss in Lung Surgery	1
	100

This list by no means includes all of the contracts which had a bearing on surgical problems, but represents only those which were assigned for administrative purposes to the Division of Surgery of the C. M. R., most of them having been recommended to the C. M. R. by the Committee on Surgery and its Subcommittees. The very extensive research programs on shock, blood, and blood substitutes were developed through special committees of the N. R. C., comprising representatives of several branches of medical science, and were administered through the Division of Physiology of the C. M. R. The work on blood-fractionation products, including fibrin foam, fibrin film, and thrombin was sponsored by these groups. Still another committee was concerned with problems of convalescence and rehabilitation, and promoted a large amount of work on the nutritional problems of surgical patients. Work on production and chemical characterization of penicillin was coördinated through a group of chemists and microbiologists, and its clinical investigation was organized and supervised by the Committee on Chemotherapeutics and Other Agents. Naturally, many surgeons participated in the latter study.

It became increasingly apparent that research in surgical problems could not be fitted into a compartmentalized scheme of organization—the solution of most of the fundamental problems of military surgery could only be approached through the coördinated efforts of scientists of virtually every classification.

It would be undesirable to attempt in one article to review all of the work performed through the surgical research program of the National Research Council and the Committee on Medical Research of the O. S. R. D. The interested reader may await publication of the full history of the activities of the C. M. R.—which will include a complete bibliography of the reports published by the individual investigators, and which will be available a few months hence. However, it seems appropriate to enter a somewhat more detailed discussion of one particular phase of the program, the integrated studies which were carried out under the sponsorship of the Subcommittee on Infected Wounds and Burns. This discussion will serve to illustrate the type of coöperative effort which is difficult to achieve in peace-time, largely because of lack of funds, but which was carried out successfully in many lines of research under the impetus of World War II.

PREVENTION AND TREATMENT OF INFECTION IN WOUNDS AND BURNS

The Subcommittee on Surgical Infections, at its initial meeting on June 6, 1940, began to make plans for a comprehensive study of chemotherapy in the control of infection in wounds. This group collaborated with the Committee on Chemotherapeutics and Other Agents in recommending to the armed services that the prophylactic administration of a sulfonamide by mouth be commenced as soon as possible after injury, particularly as a means of preventing hemolytic streptococcic infection. However, the Subcommittee was reluctant to make any recommendation governing the local use of sulfonamides in the treatment of wounds, because there were no data then available to justify this practice. It was hoped that properly controlled studies on this problem might

be completed before the outbreak of hostilities, which then seemed remote. In May, 1941—one year later, there were still no funds available to establish the needed research units, but, in response to an urgent request from the Surgeons-General, the Subcommittee recommended to them that sulfanilamide crystals be employed locally in all wounds during the interval prior to débridement, and again at the time of wound closure. This action was necessarily based solely upon the current trend of opinion of civilian surgeons, among whom a wave of enthusiasm for this procedure had begun to develop. The opportunity partially to test these recommendations in a large scale clinical and laboratory study was provided in the fall of 1941, after the establishment of the O. S. R. D. and the Committee on Medical Research. Final arrangements were then made to establish wound study units in eight teaching hospitals—Presbyterian Hospital, New York, Johns Hopkins Hospital, Baltimore, Charity Hospital, New Orleans, Cincinnati General, Henry Ford Hospital, Detroit, the Detroit Receiving Hospital and the City Hospital of Akron, where a special research unit was established by the University of Pennsylvania. To these was later added a burn-study unit at the Cook County Hospital, in Chicago. Each unit was equipped with laboratory facilities and personnel for bacteriologic and other clinical laboratory work on the patients under study; in each unit there was a responsible investigator and one or more clinical assistants, who examined all of the accident cases upon admission, observed their primary surgical treatment, directed the chemotherapeutic treatment and the bacteriologic studies, and compiled very detailed records of each case on special forms supplied to all of the units. These records were then submitted to the central statistical office of the project which was maintained under Doctor Meleney's direction in New York. The assessment of the end-results as far as infection was concerned was based on *clinical* rather than *bacteriologic* evidence of infection in the wound. The compilation of complete bacteriologic data on each wound was made simply for the purpose of attempting to relate the end-results of chemotherapy to the bacterial flora of the wound, and to find out what changes in flora might be taking place during the course of treatment. The responsible investigators and their clinical assistants met in Washington with the Subcommittee at intervals of about two months to present the results from their respective units and to discuss the implications of their experiences. Several methods of chemotherapeutic management were evaluated in each of the three main categories of lesions under study, soft-part wounds, compound fractures and burns. One group of patients in each unit received sulfadiazine systemically and a mixture of equal parts of sulfanilamide and sulfadiazine locally; another group received systemic sulfadiazine and sulfanilamide locally; still another received only the systemic drug. Finally, and very fortunately, there was a group which was given only the same standardized surgical treatment provided to all of the patients, and no chemotherapy, either systemically or locally.

By the end of 1942, after one year of operation of the wound study units, something over 1,000 completely studied cases were on file. The analysis of

this material, which has been reported in detail,[2] brought out the following facts:

1. Factors tending to delay or interfere with wound repair, such as extensive tissue trauma, incomplete débridement, or improper or ill-advised closure with tension, residual dead-space, or implantation of foreign materials, will always predispose to the development of infection in accidental wounds.

2. The use of chemotherapeutic agents in any combination and by any route does not prevent local infection of the wound when these predisposing factors exist.

3. Chemotherapeutic agents are probably of great value in preventing invasive sepsis and death from infection following accidental wounds.

In the interest of completeness the study of contaminated wounds was continued in some of the units for approximately one more year, and several new categories of prophylaxis were added, including local sulfathiazole, and systemic penicillin. However, the final report[3] does not offer any essential modification of the conclusions reached after the initial year. It is of interest that the collected experience from all the groups served only to fortify the impressions reached independently by the investigators on the basis of their individual experiences. The Subcommittee brought together individuals of widely differing points of view regarding the problem under study. Many hours were spent in discussion and brisk arguments over questions such as the significance of the statistical aspects of a study in which so many variables were involved, or the number of different categories of treatment which it would be feasible to employ; over how a wound should be cleansed or débrided, and what constituted suitable conditions for primary closure of a wound. However, the series of cases became large enough to permit statistical demonstration of adequate degrees of similarity between the respective treatment groups, and differences of opinion which were not resolved through increasing experience and accumulation of data were found to be essentially without importance.

In spite of the unequivocal results obtained in this study, the Subcommittee was reluctant to recommend to the armed services the complete abandonment of prophylactic chemotherapy. There was little evidence forthcoming from the combat areas to suggest that the local implantation of sulfonamides was harmful, apart from the danger of misplaced confidence in "magic drugs," with resulting compromises in adequacy and timing of surgical treatment. It is true that there were occasional reports of severe urinary tract complications from the administration of sulfadiazine. However, it was recognized that the factor of delay in treatment of civilian accident cases was far less important than the same factor under military combat conditions—and it seemed possible that prophylactic chemotherapy administered to the casualty during transport to a forward surgical unit might possess a measure of value not necessarily demonstrable in the civilian experiment. Therefore, the data from the study were made fully available to the Surgeons-General, and the final decision was left to them as to future military policy in regard to prophylactic chemotherapy under combat conditions. The following quotation from the section on

"Chemotherapy" in the most recent bulletin on wound management from the Office of the Surgeon-General, U. S. A.,[4] indicates that the final evaluation of prophylactic chemotherapy under combat conditions was not dissimilar from that gained through the civilian study:

"Chemotherapy: No presently available chemotherapeutic agent can sterilize a contaminated or infected war wound. Neither penicillin nor the sulfonamides can prevent the ultimate septic decomposition of dead tissue or contaminated blood clots. Sulfonamides administered systemically are effective in the prevention and control of invasive hemolytic streptococcal infection but are ineffective in the control of staphylococcal or invasive clostridial infections. Penicillin is effective against hemolytic streptococci and staphylococci and, in addition, prevents the spread of clostridial infection from a focus of affected tissue. The effectiveness and limitations of chemotherapy are established sufficiently to attribute poor results to errors in surgical technic or judgment rather than to drug failures.

(a) "The concomitant use of sulfonamides and penicillin is unnecessary. The use of sulfonamides as a supplement to penicillin therapy contributes only the risk of untoward reactions and complications. There is no clinical evidence of synergism with the two agents.

(b) "The routine local use of chemotherapeutic agents has been abandoned. Penicillin may be instilled into serous cavities or major joints to complement the initial or subsequent surgical management of injuries in these regions. Repeated dressings solely for the purpose of application of antibacterial agents contribute to persistent wound suppuration with aerobic wound pathogens.

(c) "Systemic chemotherapy is an adjuvant to the surgical management of a contaminated or infected wound. It does not offset the hazard of residual dead space or improper drainage."

It is of interest that the conclusions derived from experience of medical officers in war theaters should have so closely paralleled the results of the study in civilian practice.

EVALUATION OF PENICILLIN IN ESTABLISHED SURGICAL INFECTIONS

During the second year of the operation of the wound study units there was a gradual transfer of emphasis from the problem of prevention of infection in accidental wounds to the problem of *treatment* of established infections, using the same research facilities and personnel, but with the addition of special units at the Boston City Hospital, Cook County Hospital, in Chicago, the Hospital for Joint Diseases, in New York, and the University of California Hospital, in San Francisco. It had become apparent that one important reason for the ineffectiveness of sulfonamides in wound prophylaxis was the relative resistance of the *Staphylococcus aureus* to the action of these drugs. By January of 1943 the supply of penicillin available for clinical research had reached levels which permitted large scale investigation, and adequate quantities were made available to each of the study units. Arrangements were made between the Committee on Medical Research and the Medical Department of the Army to permit the establishment of a special unit to investigate the use of penicillin in connection with the treatment of ununited infected compound fractures at the Bushnell General Hospital, under the direction of Dr. Champ Lyons, a

member of the Subcommittee on Surgical Infections. After an encouraging preliminary experience, a much larger unit was developed by the Army in the Halloran General Hospital, also under the direction of Major Lyons, and large numbers of suitable cases were sent for treatment at this Center. As a result of this highly successful venture in Army research the basic principles governing the usefulness and limitations of penicillin in treatment of infected compound fractures were formulated, and attention was called to the importance of metabolic and nutritional derangement in patients with chronic sepsis.[5]

At about the same time, Dr. Allen O. Whipple was despatched by the Committee on Medical Research to visit the North African Theater and Great Britain, in order to obtain information regarding the preliminary investigations on penicillin in war wounds which were then in progress, chiefly at the hands of British investigators. In the report which Doctor Whipple submitted upon his return, he described the difficulties involved in conducting properly controlled studies within a military Theater, but stated that penicillin could unquestionably be expected to increase the scope and effectiveness of surgery in treating compound fractures, and urged the mass production of the drug. It was pointed out that the saving of mortality and morbidity would amply justify the use of the large amounts of penicillin required for pre- and postoperative treatment of the more serious cases. There is no doubt that this report of Doctor Whipple, transmitted through the C. M. R. to the War Production Board and the penicillin manufacturers, played an important part in stimulating penicillin production to the point where ample supplies were available for treatment of casualties occurring in the invasion of Normandy, nine months later.

Meanwhile, the civilian research units continued to gather experience in the use of penicillin in the treatment of all types of surgical infections, including staphylococcic bacteremia and acute and chronic osteomyelitis, empyema, meningitis, and related disorders. A full abstract of each patient treated was sent to Dr. Chester S. Keefer, of Boston, who directed the civilian research program on penicillin for the Committee on Medical Research and the National Research Council. The experiences of each study unit were presented for discussion at bimonthly meetings of the Subcommittee on Surgical Infections. The result of this collaborative effort was that, by the time penicillin could be made generally available for civilian use, the general principles regarding selection of cases, dosage, indications for combined surgical treatment, and the limitations of the drug, could be published for the guidance of the medical profession.[6]

TREATMENT OF BURNS

The evolution of burn treatment during the war saw the gradual abandonment of tanning methods and the substitution of a local treatment consisting in the application of a bland padded pressure dressing. An important chapter in the surgical research program under the C. M. R. and the N. R. C. is the story of its part in furthering this trend, which showed itself in military as well

as in civilian surgery. Soon after Pearl Harbor it was recognized by both Army and Navy that tanning methods were poorly adapted for use under military conditions. However, the choice of alternative methods was difficult to make, so many and varied were the technics advocated by different individuals—ranging from sulfonamide films, ointments, and powders, to paraffine sprays and Bunyan bags. This was the problem which was presented to the Subcommittee on Burns, when it was organized under Doctor Whipple's chairmanship in July, 1942. By that time the wound study units of the Subcommittee on Surgical Infections had been in operation for several months, and a large number of burn cases had been treated by a variety of methods, including tannic acid. It had been recognized that tanned burns showed a high incidence of infection, and that such infections were in no way prevented by the use of prophylactic sulfonamides. The severity and chronicity of infections in burns was found to be largely related to the extent of the areas of full-thickness injury and serious infections were infrequent in second degree burns treated by other than tanning methods. This experience was made available to the Subcommittee on Burns. The facilities of the wound study units were offered to the Committee for service as testing Centers for whatever new forms of treatment it might recommend for trial. This close collaboration led ultimately to the merging of the two Subcommittees in December, 1943, with Doctor Whipple becoming chairman of the combined group.

As soon as the unsuitability of tanning methods for treatment of burn casualties of warfare became clearly demonstrated, the Subcommittee recommended to the Surgeons-General in October, 1942, that tanning of burns be discontinued and that procurement of tannic acid preparations be stopped. Although they were not yet prepared to suggest an alternative method, the group had been impressed with the results obtained by Doctor Sumner Koch, and his colleagues, with the use of padded pressure dressings, and by the soundness of the theoretic principle of treating the burn like any other large open wound.[6]

The Boston Cocoanut Grove Fire, in November, 1942, then provided an opportunity dramatically to demonstrate the practical usefulness of this method in handling large numbers of burn casualties. Many valuable data on burns were gathered by the burn-study units at the Massachusetts General and Boston City Hospitals. The Subcommittee on Burns thus felt justified, early in 1943, in recommending that petrolatum gauze and padded pressure dressings be employed in definitive treatment of burns, and, as far as possible, in first aid management as well. They suggested that chemotherapeutic agents might be administered systemically as a means of controlling invasive infections—but the local application of sulfonamides was not recommended as a routine measure in fresh burns.

During the ensuing months much attention was given to the choice of the most suitable materials for direct application to the burned area beneath the pressure dressing. Several types of bland greases and emulsions, zinc peroxide ointment, penicillin and sulfonamide ointments, dry gauze, nylon and rayon

fabric—all were tested—both on clinical burns and on experimental donor-sites. It cannot be said that unanimous agreement was ever attained on the choice of the best local agent—but the very persistence of disagreement among individuals continuously associated in this study was a fairly convincing demonstration that the main consideration was *"nihil nisi bonum"*—and that in the *second-degree burn,* the choice among any of several *harmless* materials was unimportant. It may be said, however, that the usefulness of local sulfonamide was never clearly demonstrated.

Agreement to this extent permitted directing attention more specifically at the problem of local treatment of the full-thickness burn. The worst infections, the most prolonged morbidity, and the most severe instances of nutritional deficiencies were always associated with burns showing extensive third-degree involvement.

The approach to this phase of the burn problem followed two lines—first, the attempt at early surgical excision of the burn slough—and second, the development of chemical methods of hastening the separation of irreversibly damaged skin. Surgical excision and grafting proved feasible if the burn was of limited extent, and if ample quantities of blood were transfused into the patient at the time of the operation. However, the most promising technic for general use in third-degree burns appeared to be the employment of dressings of pyruvic acid in starch paste. This method reached a practical stage of development too late to be employed in the treatment of burns in military hospitals, but it stands as an advance which will be carried forward into civilian practice. When the burn slough can be entirely removed within ten or twelve days of the injury, as is frequently possible with this method, complete coverage with skin grafts can be performed at once, the prolonged phase of suppuration and protein loss is avoided, the further destruction of islands of epithelium through infection is prevented, and the development of scar tissue and contractures is minimized.

The scope of this review will not permit any discussion of the large amount of work which was carried out in many centers on the physiologic aspects of burn treatment—studies which provided both description, and appropriate treatment, of the imbalances in fluid, electrolytes, plasma protein, hemoglobin, nitrogen, and vitamins which accompany the severe burn. Responsibility for work on this aspect of burns was shared with the groups which were primarily concerned with research on shock, blood substitutes, and nutrition.

A valuable opportunity for a large scale demonstration of the soundness of the principles evolved from this collaborative program on burns was permitted at the time of the Hartford circus fire, in July, 1944, when the staff of the Hartford Hospital cordially invited representatives of the Subcommittee on Infected Wounds and Burns to visit their emergency burn wards, and to offer advice concerning the regimen to be employed. It is probably significant that only three deaths occurred among the fifty-four severely burned patients admitted to the Hartford Hospital the evening of the fire. Much credit for this achievement must be assigned to the splendid way in which the hospital staff

was organized to handle such a catastrophe, and to the promptness and efficiency with which shock was combatted with plasma and whole blood.

OTHER SURGICAL RESEARCH PROJECTS

This article has reviewed only those phases of the surgical research program which were collaborative team projects. No attempt will be made to cover the many important studies which were carried on by individual groups. The research on wound ballistics at Princeton, and at Yale, represents an application to the age-old problem of missile wounds the most modern technics of mechanical, optical, and electronic biophysics. The Department of Radiology at the University of Chicago developed and placed on a practical basis devices for controlling automatically the duration of roentgenray exposures so as to yield films of optimal contrast density. At Columbia a team of investigators studied the tissue reactions and the range of usefulness of absorbable cellulose as an hemostatic agent, and still another group produced a relatively simple method for nonsuture anastomosis of blood vessels. The problem of frost-bite injury and trench foot was studied at several institutions, and the pathogenesis and treatment of these lesions was further elucidated. A team of biologists and physicists at Massachusetts Institute of Technology worked for three years on the preparation from purified animal collagen of a highly standardized absorbable suture material, of great promise for future development. The extensive program of research on cerebral concussion, and peripheral nerve repair under the Subcommittee on Neurosurgery, would require a separate article in itself. Finally the problems of the amputee were taken up by a special committee under the National Research Council, with financial support from the C. M. R. This committee first surveyed the entire field of prosthetic devices and then developed sub-contracts for research designed to make available more comfortable and serviceable artificial limbs. This work is now being continued under the National Research Council with combined support from the Veterans Administration and the War Department.

There were unquestionably many mistakes made, and numerous difficulties encountered, which have not been described in this account. Many of the mistakes came about as the result of civilian ignorance of military conditions, and it must be remarked that the war was almost over before the civilian investigators were permitted to become even partially familiar with the details of some of the medical problems in the combat zones. The work of civilian investigators could have been much better focused on the actual problems of the Theater medical officers if there had been opportunity earlier in the war for direct exchange of information between individuals working on similar problems at home and abroad, respectively. Efforts to obtain wide distribution of research progress reports to individual medical officers in the field were never successful. Difficulties arose from the shortage of trained professional and technical personnel and from the fact that most of the investigators were carrying unusually heavy loads of teaching responsibility in addition to their research work. However, most of those who found themselves occupied in the

war-time research program, whether as Committee members, administrators, investigators, or assistants, felt that their tasks in the effort of total war were significant for peace as well as for war, and the record of accomplishment is one to which they may perhaps point with some degree of satisfaction.

REFERENCES

(Note: This bibliography is confined to references to coöperative team projects. A full bibliography of individual publications will appear in the forthcoming history of the Office of Scientific Research and Development.)

[1] Data supplied by Dr. George B. Darling, Executive Secretary, National Academy of Sciences, Washington, D. C.

[2] Meleney, F. L.: ANNALS OF SURGERY, **118**, 171, 1943; *idem:* Surg., Gynec., & Obstet., **80**, 263, 1945.

[3] Meleney, F. L.: To be published.

[4] Surgery Consultants Division, Office of the Surgeon-General. Bull. U. S. Army Med. Dept., **4**, 245, September, 1945.

[5] Lyons, C.: J. Am. Med. Assoc., **123**, 1007, 1943.

[6] Committee on Chemotherapeutics and Other Agents, Division of Medical Sciences, National Research Council. J. Am. Med. Assoc., **122**, 1217, 1943.

THE EFFECT OF PENTOTHAL SODIUM ON MEAN ARTERIAL BLOOD PRESSURE IN THE PRESENCE OF HIGH SPINAL CORD PARALYSIS

FERDINAND F. MCALLISTER, M.D.

NEW YORK, N. Y.

FROM THE DEPARTMENTS OF PHYSIOLOGY AND SURGERY, COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK, N. Y.

IN 1941, Kees[1] reported that spinal anesthesia could be supplemented satisfactorily with pentothal sodium. This and other favorable reports[2, 3, 4] have led to an increasing use of the intravenous barbiturates in conjunction with spinal anesthesia. In view of this, and because another anesthetic agent (ether)[5] is known to act unfavorably on blood pressure when the spinal cord

TABLE I

THE MEAN ARTERIAL BLOOD PRESSURE IN THE FEMORAL ARTERIES OF NORMAL AND HIGH SPINAL DOGS AT INTERVALS DURING PENTOTHAL SODIUM ANESTHESIA

Dog No.	Preanesthetic Level	After 3 Min. of Anesthes.	After 5 Min. of Anesthes.	After 10 Min. of Anesthes.
Normals:				
129	105 mm.	140 mm.	140 mm.	140 mm.
3	115	140	140	140
4H	135	145	140	140
3B	140	170	160	160
1	120	110	105	105
Spinals:				
129	130 mm.	140 mm.	130 mm.	115 mm.
3	95	115	110	100
4H–12th d.	95	115	110	100
4H–18th d.	100	100	130	120
3B–high sp. anesthes.	105	80	95	90

CHART 1.—This record shows the effect of a fairly rapid injection of pentothal sodium on the femoral arterial blood pressure of a normal dog. With a control blood pressure of 135 mm. Hg, 9 cc. of 2 per cent pentothal sodium was injected in 25 seconds. There was an immediate drop to 85 mm. Hg and a quick return to 145 mm. Hg within 3 minutes after the start of the injection. At 5 and at 10 minutes after the onset of anesthesia the blood pressure registered 140 mm. Hg. A satisfactory anesthesia was obtained for 30 minutes. As has been pointed out in the text, there is no initial fall in pressure when the injection is given more slowly.

CHART 2.—This record shows the effect of a rapid injection of pentothal sodium on the blood pressure of the same dog as in Fig. 1 12 days after aseptic transection of the spinal cord between C6 and C7. With a control blood pressure of 95 mm. Hg, 6 cc. of 2 per cent pentothal sodium was injected in 22 seconds. There was an immediate fall to 75 mm. Hg followed by a quick return to 115 mm. Hg. At 5 and 10 minutes after the onset of anesthesia the blood pressure registered 110 and 100 mm. Hg respectively. The anesthesia lasted 45 minutes. Note the similarity between this record and that of Chart 1.

CHART 3.—This record shows the effect of the inhalation of ether for 1½ minutes on the blood pressure of the same dog as shown in Charts 1 and 2 12 days after spinal cord transection at C6 to C7. The control blood pressure was 105 mm. Hg. Within 1 minute the blood pressure had fallen to 55 and, within 2 minutes to 40 mm. Hg. Previous studies have shown that in such preparations the blood pressure remains low throughout surgical anesthesia with ether. Persistence in the administration of ether in the above case would probably have led to the death of the animal.

CHART 1

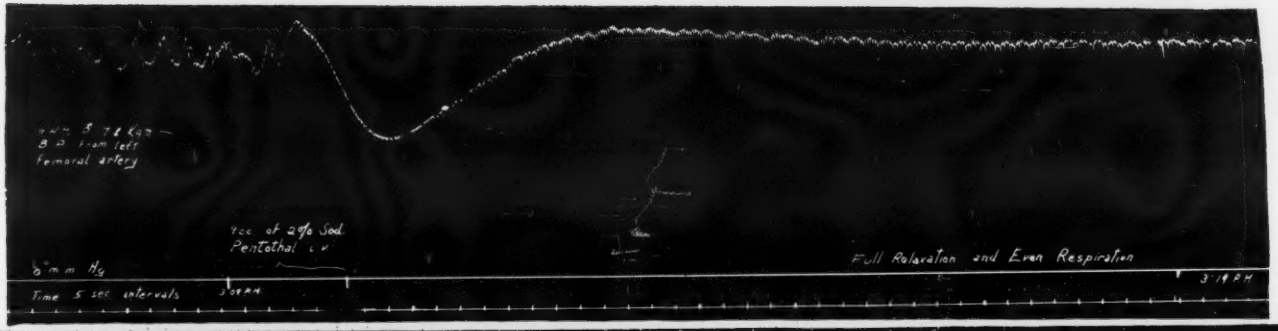


CHART 2

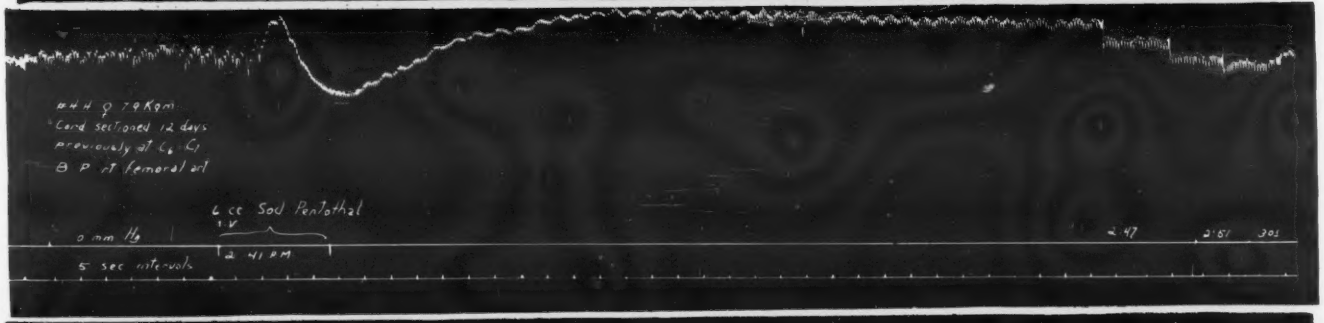
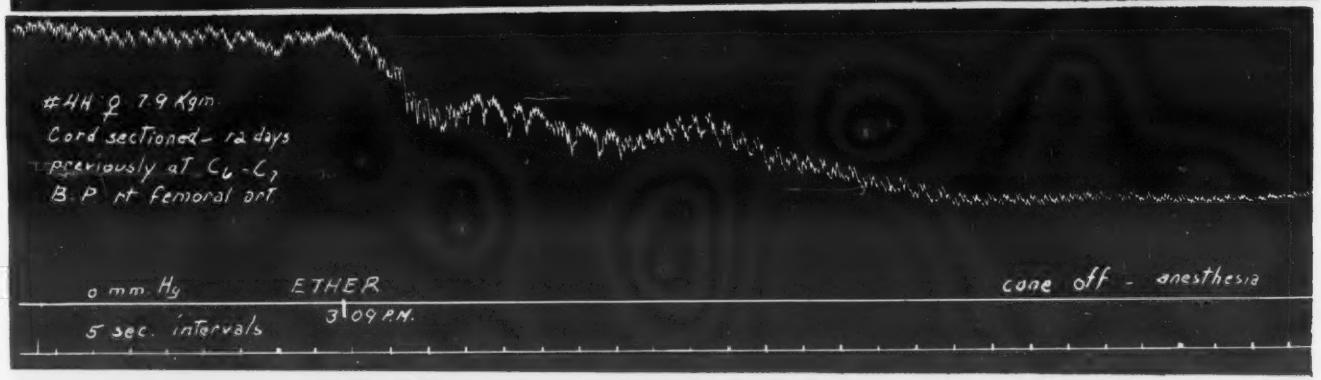


CHART 3



impulses are interrupted at D6 or above, it seemed of interest to study the action of pentothal sodium on blood pressure when the suprasegmental impulses have been eliminated high in the spinal cord either by transection or spinal anesthesia.

Method of Study.—Control determinations of blood pressure during pentothal sodium anesthesia were made on normal dogs. A cannula was inserted into one of the femoral arteries under 1 per cent novocaine local anesthesia, and the blood pressure was recorded on a kymograph, using a citrate system. Anesthesia was induced with 2 per cent pentothal sodium given in the jugular or the leg veins at variable rates of injection. The depth of narcosis was considered adequate when there was loss of consciousness, complete muscular relaxation, slow, regular respiration and lack of response to painful stimuli. The anesthesias thus administered lasted from 20 minutes to one and one-half hours.

Spinal cord transections were made aseptically in the lower cervical region between C6 and D1. The above experiments were then repeated four to 28 days postoperatively. In one animal, high spinal anesthesia (all intercostal respiration eliminated) with procaine was employed in place of spinal cord transection.

RESULTS

Controls.—In 15 experiments, the initial dose of pentothal sodium required to produce satisfactory anesthesia ranged from 185 to 258 mg. per kilogram of body weight. The rate of injection varied from 0.17 to 0.90 mg. per kilogram, per second, which is somewhat faster than that customarily used in humans. When the injection was rapid, it caused an immediate fall in arterial pressure which in some instances amounted to 70 mm. Hg (Chart 1). When the drug was given more slowly, there was no immediate fall in pressure, and, if given slowly enough to result in an excitement stage, it caused a momentary rise of as much as 60 or 70 mm. Hg. Whatever the initial response, recovery usually occurred within three minutes and the blood pressure remained close to or slightly above the preanesthetic level. When the anesthesia was light, the blood pressure tended to be somewhat elevated. The average control pressure was 117 mm. Hg. and, after 10 minutes of pentothal sodium anesthesia, the average reading was 126 mm. Hg.

Spinals.—In five experiments it was found that pentothal sodium may be given in the presence of high spinal cord paralysis without seriously altering the blood pressure (Chart 2). Although the doses of the drug used fell within the range employed on the controls, a smaller amount of pentothal was required in the same dog after high spinal cord transection (Chart 2) or while under high spinal anesthesia. As with the normal animals, a rapid injection produced an initial transitory fall in pressure and a slow injection produced a transitory rise in pressure. The average control pressure in this group was 105 mm. Hg. and, after 10 minutes of anesthesia, the average pressure was again 105 mm. Hg. Sample blood pressure readings from both groups are presented in Table I.

DISCUSSION.—The above experiments on dogs indicate that, when the function of the spinal cord has been interrupted in the lower cervical or upper thoracic region, intravenous pentothal sodium anesthesia produces no serious depression of the blood pressure. Thus, this anesthetic is quite different from ether which is known to cause a pronounced fall in the blood pressure of such animals[5, 6] (Chart 3). Experimentally, then, when the suprasegmental vasomotor control has been eliminated, intravenous pentothal is a safer anesthetic than ether.

CONCLUSION

Intravenous pentothal sodium anesthesia may be administered to dogs with high spinal cord paralysis without seriously altering the blood pressure. This is in marked contrast with ether anesthesia which, under similar circumstances, produces an abrupt and dangerous fall in blood pressure.

REFERENCES

1 Kees, P. A.: Combined Intravenous-spinal Anesthesia. Anesth. and Analg., **20,** 24–26, Jan.-Feb., 1941.

2 Sibley, W. L.: Intravenous Anesthesia Combined with Regional Anesthesia. South. M. J., **34,** 910–913, Sept., 1941.

3 Tuohy, E. B.: Clinical Use of Intravenous Anesthesia alone and in Combination with other Anesthetics. South. M. J., **34,** 42–45, January, 1941.

4 Anderson, B. M., Mousel, L. H., and Mayo, C. W.: Combined Spinal and Intravenous Anesthesia for Operations on the Colon. Surg. Gynec. and Obst., **75,** 651–656, November, 1942.

5 Root, W. S., and McAllister, F. F.: The Circulatory Responses of Chronic Spinal Dogs to Ether Anesthesia. Am. J. Physiol., **134,** 65–70, August, 1941.

6 McAllister, F. F., and Root, W. S.: The Neurogenic Control of the Circulation of Dogs under Ether Anesthesia. Anesthes., **3,** 491–506, September, 1942.

THE IMPORTANCE OF WHOLE BLOOD TRANSFUSIONS IN THE MANAGEMENT OF SEVERE BURNS

JOSEPH J. McDONALD, M.D., EDWARD F. CADMAN, M.D.,
AND
JOHN SCUDDER, M.D.
NEW YORK, N. Y.

FROM THE DEPARTMENT OF SURGERY AND THE DIVISION OF PLASTIC SURGERY, COLUMBIA-PRESBYTERIAN MEDICAL CENTER, NEW YORK, N. Y.

RECENT STUDIES in the physiology and treatment of burns have brought forth controversial views in regard to the form of replacement therapy indicated during the immediate as well as the later stages of burns. Riehl,[15] in 1925, advocated whole blood transfusions in the shock phase and in subsequent years many other investigators wrote of its advantages. However, after 1938, plasma or serum was widely accepted as the treatment of choice in burn shock. More recently, oral electrolyte solutions and whole blood transfusions, individually or in combination, have been recommended. The correct answer to the problem probably lies in the integrated use of all three agents, but to determine the amounts and the time at which each should be administered will require the critical evaluation of more extensive laboratory and clinical data. To contribute toward this goal is the purpose of the present communication.

CLINICAL MATERIAL

The ten cases selected for the present analysis suffered flame burns of from 30 to 80 per cent of their body surfaces and were treated under the direction of various members of the surgical staff of the Presbyterian Hospital, New York, between May 28, 1941 and December 3, 1944. They are not consecutive cases but include only extensive burns treated during that period upon whom sufficient data were obtainable to render them useful for comparative study. The fluid therapy in Case 8 was discussed in a previous paper.[21]

The first four cases had overwhelming burns and from the outset appeared to have little or no hope of survival but are presented as a comparison of four types of shock therapy. Of the remaining six cases, two died in the post-shock phase and four survived. They are presented mainly for the analysis of their supportive treatment during the period of healing. Table I presents a summary of the ten cases analyzed.

METHODS

Percentages of the burned areas were estimated on the basis of Lund and Browder's[10] modification of the Berkow scale. Blood volume determinations, where referred to, were done by the method of Gregerson under the direction of Dr. Dickinson Richards[14] and his associates who simultaneously studied some of the cases.

In charts of the individual cases the average daily temperature is used as a simple index of the patient's general condition during the course of treatment.

TABLE I

SUMMARY OF CASES

Case	Sex and Age	Per Cent of Burn: Total	3°	2°	Shock Therapy	Post-shock Therapy	Outcome
1	M—64	80	60	20	1500 cc. oral lactate in 4.5 hours (partially vomited)		Death in 4.5 hours
2	F—45	60	45	15	2000 cc. serum, 2000 cc. saline, 2000 cc. plasma } I.V. in 6 hours		Death in 6 hours
3	F—73	30	25	5	800 cc. saline I.V. + 1500 cc. oral lactate } in 15 hours		Death in 15 hours
4	F—74	75	50	25	1500 cc. blood, 1000 cc. plasma, 3000 cc. saline I.V. + 1500 cc. lactate P.O. } in 36 hours	1700 cc. plasma in 4 days	Good recovery from shock; death on the sixth day
5	F—32	42	30	12	1000 cc. blood, 3000 cc. plasma, 1500 cc. saline I.V. + Fluids ad. lib. P.O. } in 72 hours	Small infrequent transfusions: 1800 cc. blood, 1250 cc. red cells in 5 weeks	Good recovery from shock, but progressive anemia and hypoproteinemia with death on the 37th day
6	F—29	44	34	10	9000 cc. lactate and saline, and 2000 cc. other fluid by mouth in 24 hours; (4300 cc. vomited)	Oral R only until 14th day; 3000 cc. blood, 500 cc. red cells in next 11 days	Severe red cell and protein deficits not controlled by late transfusions; death from pulmonary complications on the 25th day
7	M—25	51	33	18	3500 cc. plasma, 3000 cc. saline I.V. in 6 days	Frequent transfusions: 4300 cc. blood in 8 days, 2500 cc. blood in next month	Post-shock anemia quickly corrected; complete healing in 3.25 months
8	M—32	53	7	46	4000 cc. serum, 4500 cc. saline I.V. in 48 hours	Frequent transfusions: 6500 cc. blood, 2000 cc. plasma in 1 month	Progressive healing: discharged in 4.5 months
9	F— 9	50	35	15	900 cc. plasma, 1200 cc. saline I.V. in 3 days	Frequent transfusions: 3660 cc. blood, 1460 cc. red cells in 5 weeks	Anemia and hypoproteinemia quickly corrected; complete recovery in five months
10	F—27	50	44	6	10,000 cc. plasma, 5,000 cc. glucose I.V. in 5 days + NaCl tablets P.O.—10 Gm./day	Frequent transfusions: 5,500 cc. blood, 500 cc. red cells, 1,100 cc. plasma in 5 weeks	Good healing and recovery from hypoproteinemia after anemia was overcorrected; 8 months in hospitals

Changes in the plasma protein concentrations and in the hematocrit or erythrocyte counts are recorded. The type and volume of replacement therapy is shown in the form of blocks at the base of the charts. Additional data on the electrolyte intake and output, and plasma electrolyte concentrations on six of the cases were done according to acceptable methods.[20] All patients transfused were given blood of their individual group and the Rh factor was determined for each except in Case 8.

ANALYSIS OF SHOCK THERAPY IN OVERWHELMING BURNS

Case 1.—E. J., No. 735714, (Chart I), a 64-year-old Negro garage worker was admitted March 2, 1944, shortly after receiving a burn of 80 per cent of his body surface when his clothing had been ignited by the explosion of a can of gasoline. Intense hemolysis was noted in the initial blood samples. Morphine was given for pain and after a minimal cleansing his wounds were covered with a pressure dressing over a base of ointment gauze. While the dressing was being applied a nasogastric tube was passed and M/6 sodium lactate solution was administered through the tube, *much of which was vomited.* The patient was oriented and rational upon admission with a blood pressure of 150/84 but he soon became restless and then comatose, and died in burn shock four hours after admission. No intravenous therapy was given.

COMMENT.—This case illustrates the usual course of an overwhelming burn in which no effective shock treatment is given. It is noted that the plasma sodium and chloride values were normal at the time of admission and at death, but acidosis was not controlled. The hemoglobinemia and elevated plasma potassium indicate destruction of red cells which probably occurs in and adjacent to the burned area.

Case 2.—G. E., No. 692081 (Chart II), a 45-year-old housewife who was extensively burned on November 10, 1942, when her bed clothing caught fire while she was smoking in bed in an intoxicated condition. Sixty per cent of her body surface was involved (Fig. 1) and deep hemolysis was noted in the admission blood samples. A variety of local ointments and pressure dressings were applied to the wounds. Replacement therapy included 2,000 cc. of serum and 2,000 cc. of normal saline by vein within five hours. Hemoconcentration did not occur and blood pressure was maintained. As a fall in hematocrit was noted whole blood was ordered, but before it could be given the patient expired. Autopsy revealed acute pulmonary congestion, edema of the pharynx and epiglottis, and the trachea and bronchi filled with mucinous secretions.

COMMENT.—This patient apparently suffered moderate smoke burns of the upper respiratory passages and death resulted from drowning in her own secretions. The rapid infusion of saline may have been a contributing factor to the edema and hypersecretion found in the respiratory tract at autopsy.

Case 3.—C. D., No. 760218, (Chart III), a 73-year-old chronically ill white woman who was admitted October 12, 1944, shortly after suffering a deep burn of the right side of her body. She had been smoking in bed while intoxicated and the bed clothing had been ignited by a cigarette held in her right hand. Being unable to move because of severe arthritis she was exposed to the flames for several minutes before help arrived. The burned flesh was charred and deeply indurated (Fig. 2). Initial blood samples showed intense hemolysis and the admission urine obtained by catheter resembled Burgundy wine from hemoglobinuria. An ointment gauze pressure dressing was applied to the wounds, 2,000 cc. of plasma and 800 cc. of normal saline was administered by vein and 1,800 cc. of M/6

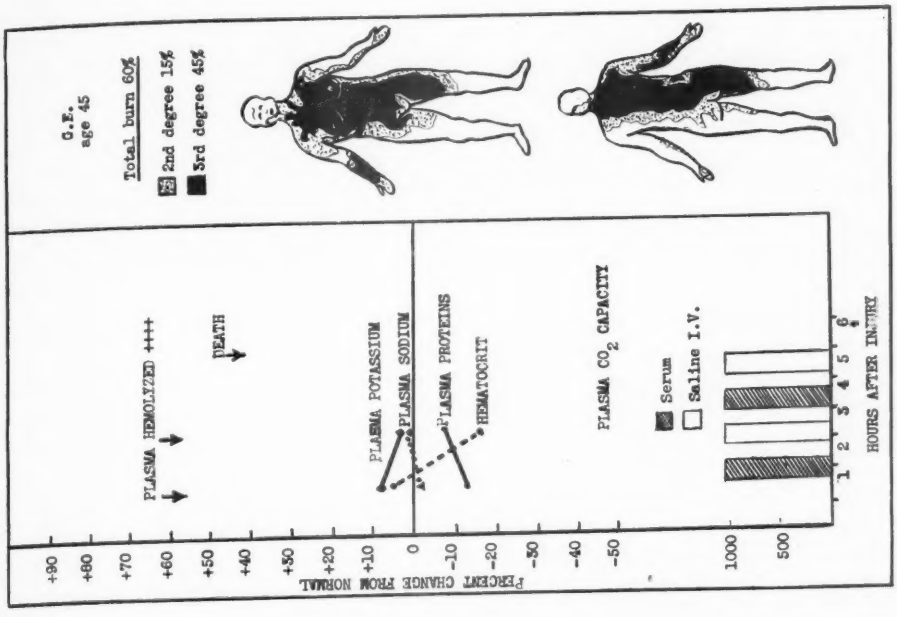


CHART II.—Treatment and course of Case 2.

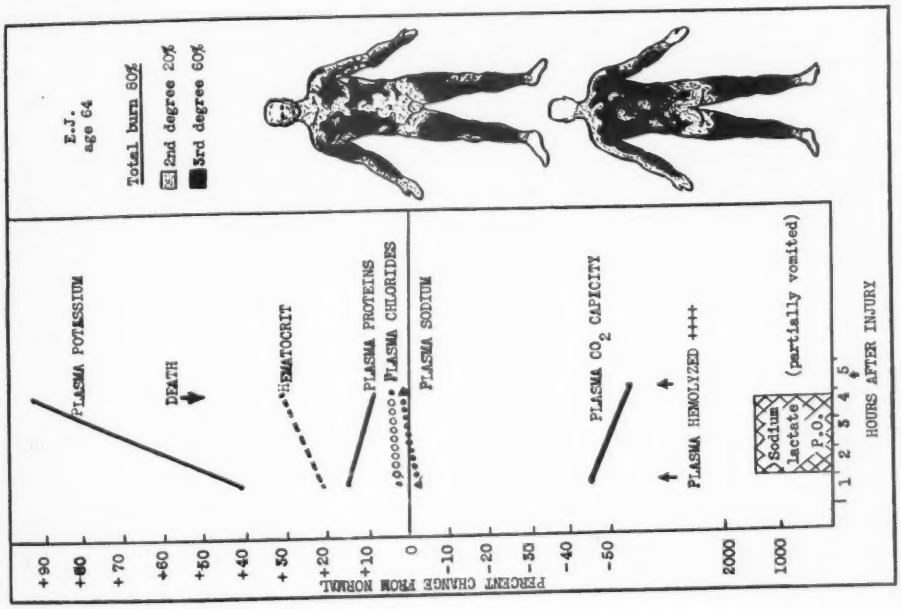


CHART I.—Treatment and course of Case 1.

lactate solution was given by nasogastric tube. No further urine was obtained and the patient expired 14 hours after admission. Additional information revealed she had been a chronic alcoholic, luetic, diabetic, hypertensive and had been confined to her bed for a year.

COMMENT.—Although only 30 per cent of the body surface was involved in this case, the tissue destruction was obviously very deep, and this injury added to her debilitated state was considered an overwhelming insult. Her survival time was comparable to that reported by Moyer, and his associates,[4] for severely burned animals treated with serum by vein and chloride-bicarbonate solution by mouth.

Case 4.—L. S., No. 765044, (Chart IV), a 74-year-old housewife was admitted November 27, 1944, shortly after sustaining a flame burn involving 75 per cent of her body surface. Her clothing had been ignited by an accident with cleaning fluid at home. Hemolysis was present in early blood samples. Morphine was given for pain, and the wounds were hastily cleansed of loose débris and covered with an ointment gauze pressure dressing. Replacement therapy during the first 12 hours included 1,000 cc. of whole blood, 500 cc. of plasma and 1,150 cc. of normal saline by vein and 1,500 cc. of M/6 lactate solution by stomach tube. On the following day an additional 500 cc. of blood, 500 cc. of plasma, 2,000 cc. of normal saline, 300 cc. of 5 per cent saline and 1,000 dog units of eschatin were given by vein and 1,750 cc. of lactate solution by mouth, about 1,000 cc. of which was vomited. The urinary output during the first 36 hours was 740 cc. and thereafter averaged about 1,000 cc. per day until her death on the sixth day. The patient remained rational and surprisingly comfortable for the first five days. She was digitalized because of the threat of cardiac failure. No anemia developed but there was a moderate fall in plasma protein concentration in spite of three additional infusions of plasma. Though no autopsy was obtained, death appeared to result from physiologic exhaustion rather than from the failure of any one specific organ or system.

COMMENT.—The use of whole blood combined with plasma, saline and oral electrolyte solution in the early stages succeeded in prolonging life in this

---

FIGS. 1 and 2.—Cases 2 and 3 on admission, each with charred skin burned to a depth of 3 to 4 cm. Blood samples showed intense hemolysis in both cases.

FIGS. 3 and 4.—Case 5: General view on admission and detail of right thigh at time of death 37 days later showing necrosis of the fat and erosion of the wound edges which resulted from inadequate treatment.

FIGS. 5 and 6.—Case 9: Anterior view 16 days after injury and dorsal aspect of trunk wound two weeks later at time of homografting. Large frequent blood transfusions were used throughout this critical period.

FIGS. 7 and 8.—Case 10: Triple dye eschar intact one month after injury, and massive but healthy granulating surface partially covered with homografts ten weeks later; progress occurred only after over-correcting her anemia.

1

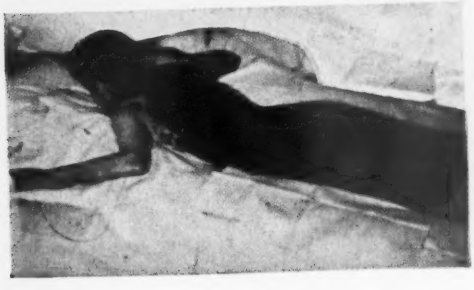
2

3

4

5

6



7

8

UNIV. OF MICH.

elderly patient with an overwhelming burn. The acidosis was corrected and anemia was prevented. Treated by other methods burns of this magnitude are usually fatal within 24 hours.

THE RATIONALE FOR GIVING WHOLE BLOOD TRANSFUSIONS AND ELECTROLYTE SOLUTIONS IN BURN SHOCK

The importance of electrolyte therapy was revived in 1943 by Rosenthal[17] who demonstrated that isotonic sodium chloride solution given orally was more efficient than intravenous plasma in controlling burn shock in mice. In 1944, Fox[7] reported a clinical study of this method using oral sodium lactate solution. In the same year Moyer, Coller, Iob, Vaughan and Marty[12] published the first comprehensive comparative study of the effectiveness of electrolytes, serum and blood, used separately and in various combinations to treat shock in severely burned dogs. Their experiments demonstrated that the combination of blood by vein and a saline-bicarbonate solution by mouth was effective while blood or electrolyte solution alone, or serum in combination with electrolyte failed.

In 1945, Abbott, Meyer, Hirshfeld and Griffin[1] confirmed Moyer's work and demonstrated that the anemia which tends to develop during the convalescent period could be prevented if whole blood was given early. In a clinical evaluation of these principles Abbott, Pilling, Griffin, Hirshfeld and Meyer[2] also concluded that whole blood transfusions plus electrolyte solution by mouth was an effective method of combating burn shock, and that this form of therapy will alleviate the anemia which is usually seen during the period of convalescence.

In a simultaneous report, Evans and Bigger[6] used large amounts of whole blood for treating shock in 32 severely burned patients and found it could be given safely in the presence of marked hemoconcentration, and when given in adequate amounts secondary anemia was regularly avoided. Blood-volume studies by these authors, made soon after the burn, indicate a significant decrease in circulating red cell mass and they feel this accounts for a considerable portion of the anemia which usually appears after burn shock but is masked during the period of hemoconcentration.

Even during the years when plasma or serum was generally used in treating burn shock many clinicians never entirely gave up the use of whole blood and were cognizant of its importance as mentioned in the writings of Harkins,[9] Duval,[5] Scudder,[20] and Brown and McDowell.[4]

The indication for whole blood is to replace blood loss. In shock from severe burns the changes in hemodynamics are equivalent to those of a massive hemorrhage combined with an additional loss of water and electrolytes (dehydration) and are not simply those of a plasma 'leak' as is often assumed. Schievers,[18] in 1936, working with rabbits demonstrated a fall in total blood volume to approximately 50 per cent of normal following a severe burn and pointed out that this deficit included the loss of red cells in almost the same proportion as plasma loss.

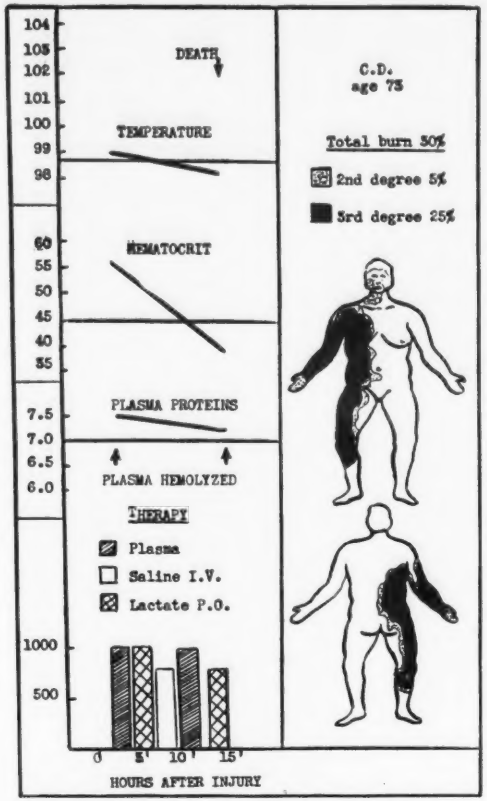


CHART III.—Treatment and course of Case 3.

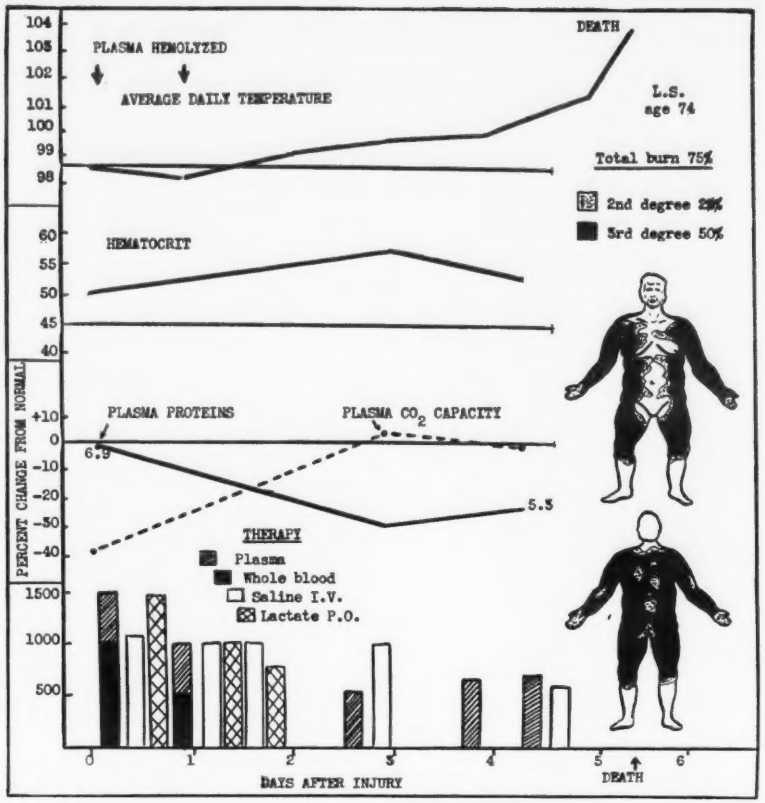


CHART IV.—Treatment and course of Case 4.

The mechanism of the loss of red cell mass from the circulation involves a number of causes. The destruction of red cells by heat with liberation of hemoglobin and potassium was demonstrated in 1884 by Von Schjerning who also pointed out the toxic effects of excess potassium in the circulation. Other partially damaged cells may fragment when exposed to the alterations in osmotic pressure which result from changes in water, electrolyte and plasma protein concentrations, thus further contributing to the hemoglobinemia and hemoglobinuria frequently seen early in extensive burns particularly where there has been deep tissue damage.[9] Evans and Bigger[6] believe the erythrocyte loss is due mainly to sludging or trapping of red cells in capillaries in and adjoined the burned tissues. Others[1, 8] have shown that congestion of large and small vessels and small hemorrhages in the damaged areas account for whole blood loss from the circulation. Preëxisting anemia is another factor which may add to the deficit in some cases.

The severity of the blood loss during the early phase of severe burns in patients has been graphically illustrated by Evans and Bigger.[6] The total loss in circulating blood volume estimated in nine of their cases ranged from 1,200 cc. to 2,500 cc. (25 to 50 per cent of the circulating blood volume of the average adult) and the per cent of red cell mass in the fluid lost from the circulation varied from 7 to 55 per cent, with an average of 37.5 per cent. In other words, the average fluid lost from the circulation was equivalent to slightly anemic blood. Assuming a normal hematocrit of 45, and a deficit of red cell mass amounting to 37.5 per cent of the fluid lost from the circulation in a severe burn, one would theoretically have to administer four parts of blood to one part of plasma to restore a normal balance. Since there is a tendency to progressive anemia in burns and since the body has no significant stores of hemoglobin but is able to mobilize considerable reserves of plasma protein, the argument for using whole blood entirely in place of plasma early in severe burns has a sound theoretic basis. Such massive transfusion therapy has been made possible with the advent of blood banks and has been made safer by the elimination of transfusion reactions due to the Rh factor.

The restoration of electrolyte and water losses beyond those not replaced with transfusions can usually be accomplished safely by the oral route provided adequate transfusion therapy is also given. Our clinical observations have been in agreement with the experimental report of Moyer[13] who noted vomiting and delayed gastric emptying as a frequent complication in burn shock, but when shock was controlled by blood transfusions fluids were usually well tolerated by mouth.

Since employing sodium lactate therapy by vein or by mouth during burn shock we have observed three striking beneficial effects: (1) acidosis is more quickly controlled, as reflected by the plasma CO_2 capacity; (2) excess potassium is quickly eliminated from the circulation; and (3) urinary output is improved. However, when lactate solution is the only electrolyte given there may be a tendency to overcorrection of the acidosis even to the point of clinical alkalosis, as noted in some of our cases. In such instances the plasma chloride

concentrations tend to fall below normal. These differences in plasma electrolyte changes are graphically illustrated in the two groups of cases compared in Chart XI. It is now generally felt that the electrolyte therapy should include a mixture of lactate and saline, or bicarbonate and saline to more nearly approach the physiologic needs of the patient. Oral administration should be started as soon as vomiting has ceased.

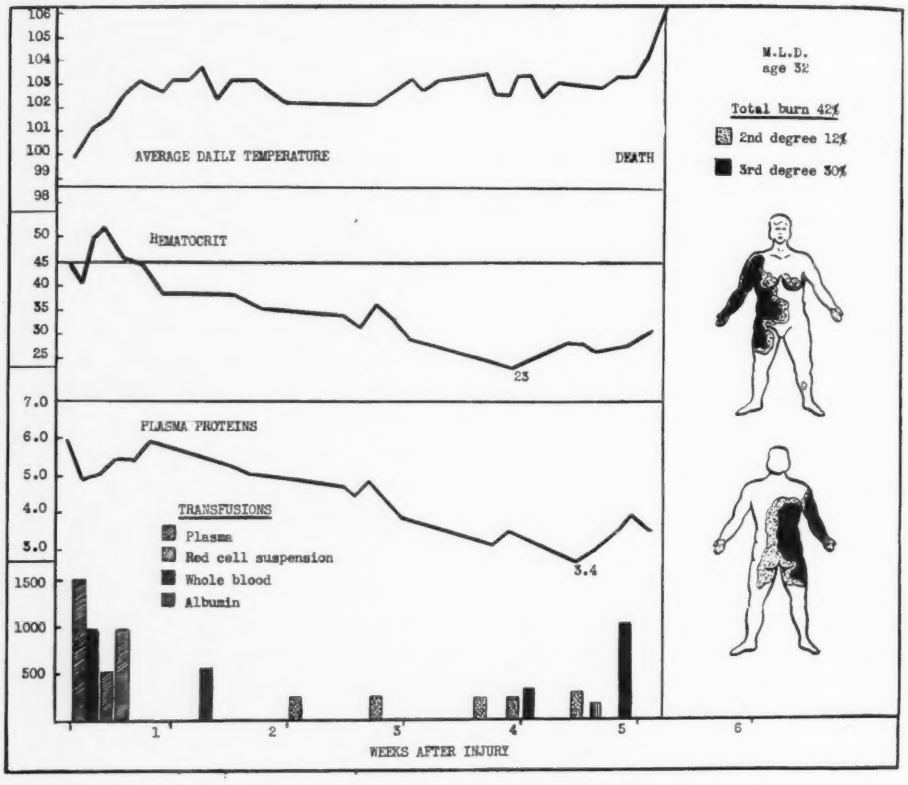


CHART V-a.—Treatment and course of Case 5.

The theoretic advantages of oral treatment alone, as proposed by Rosenthal,[17] are indeed great, but his conclusions were based on experiments on mice, animals which are physiologically unable to vomit and which possess a stomach capable of accommodating 5 per cent of their body weight in fluid (equivalent to three liters of fluid for an adult human). The advocates of oral therapy claim that a continuous drip of electrolyte solution into the stomach is adequate, but even when burn shock can be controlled by this method, the deficit in red cell mass and plasma proteins is *not corrected* as noted in the cases reported by Fox.[7] Such deficits present a serious obstacle to the patient facing the task of healing a large wound as is clearly brought out in Case 6.

ANALYSIS OF THE REPLACEMENT THERAPY IN THE HEALING STAGE OF SEVERE BURNS

Of the six cases in this group, three received initial treatment in other hospitals and were transferred to us after shock had been controlled. Some deductions may be drawn regarding the effect of early treatment on their later course, but the cases in this group are presented mainly for a comparison of the form of supportive treatment used during the post-shock period.

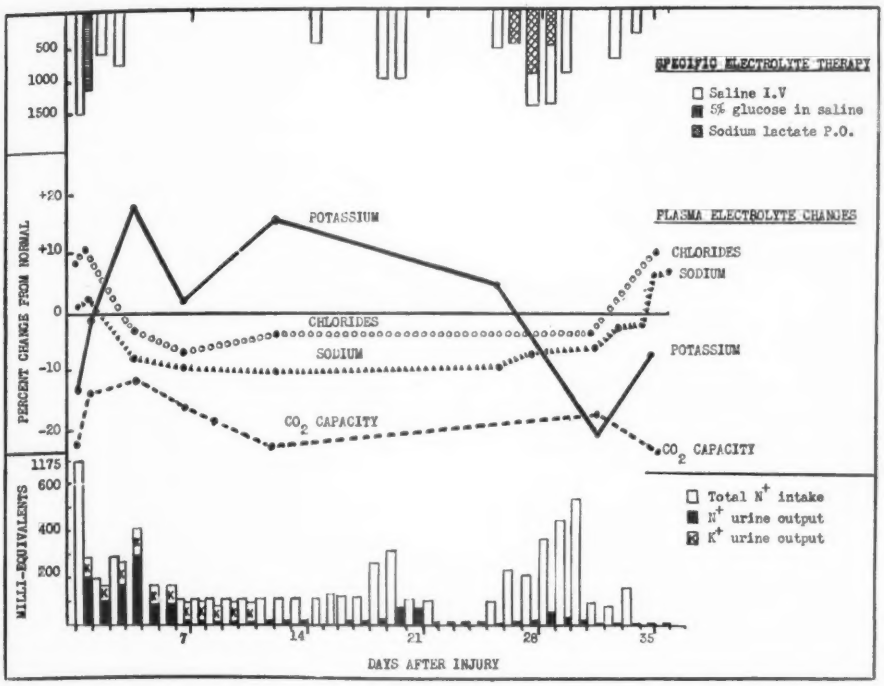


CHART V-b.—Electrolyte intake, output and plasma changes in Case 5.

Case 5.—M. L. D., No. 742683 (Chart V), a 32-year-old white woman was admitted, March 14, 1944, shortly after receiving an extensive flame burn of her right arm, trunk, buttocks and right thigh. She had fallen asleep while smoking in bed in an intoxicated condition, with resulting injury to 42 per cent of her body surface. Treatment was carried out under the direction of a combined group interested in the study of burns and shock. The wounds were dressed with a variety of ointment gauzes and an outer pressure dressing. Shock therapy included 1,500 cc. of plasma, 1,000 cc. of whole blood and 1,500 cc. of normal saline intravenously during the first 24 hours. Fluids as desired were allowed by mouth but no specific oral electrolyte therapy was given during the early course of her illness. An additional 1,600 cc. of plasma was injected on the 2nd and 3rd days. Urinary output for the first 24 hours was 1,170 cc. and averaged about 1,500 cc. per day during the ensuing three weeks. The patient's general condition was surprisingly good during the first week and her plasma proteins and hematocrit were near normal until after the first week. A gradual rise in total blood volume due mainly to an increase in plasma volume was noted during the second, third and fourth weeks and it was the feeling of the group directing her therapy that

transfusions might overload her vascular system and precipitate cardiac failure. The small infrequent transfusions given during this period were little more than enough to cover the blood withdrawn for various tests. A progressive clinical decline ensued as reflected by the steady fall in the hematocrit and plasma proteins which reached levels of approximately 50 per cent of normal by the end of the fourth week. Her wounds likewise reflected the inadequacy of the replacement therapy for a progressive destruction of tissue was noted. Areas which early in her course appeared superficially damaged became full thickness in depth and as the slough separated from the more deeply burned regions progressive necrosis of the underlying fat was observed (Fig.

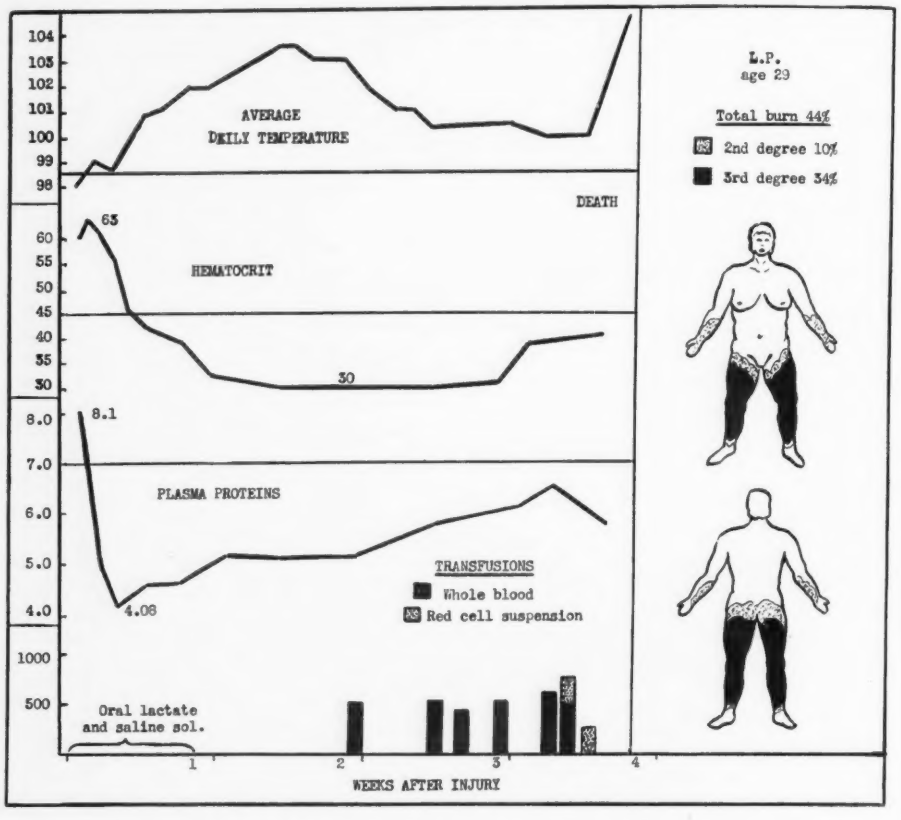


CHART VI-a.—Treatment and course of Case 6.

4). An abortive effort was made to replace her blood deficits during the fifth week, including the administration of oral lactate solution, but by this time she was too exhausted and her pathology too extensive to prevent her death which occurred on the 37th day. Postmortem examination revealed anasarca, pulmonary edema, lipid depletion of the adrenals and destruction of 42 per cent of her skin surface.

COMMENT.—The use of whole blood and plasma for the treatment of shock in this case was successful but the supportive therapy later in her course was obviously inadequate, having been withheld for the reason mentioned above.

The forcing of electrolytes late in her course, when anemia and hypoproteinemia were severe, was probably ill-advised for raising her plasma sodium and chloride levels to above normal (Chart V-b) may have contributed to the anasarca and pulmonary edema found at autopsy.

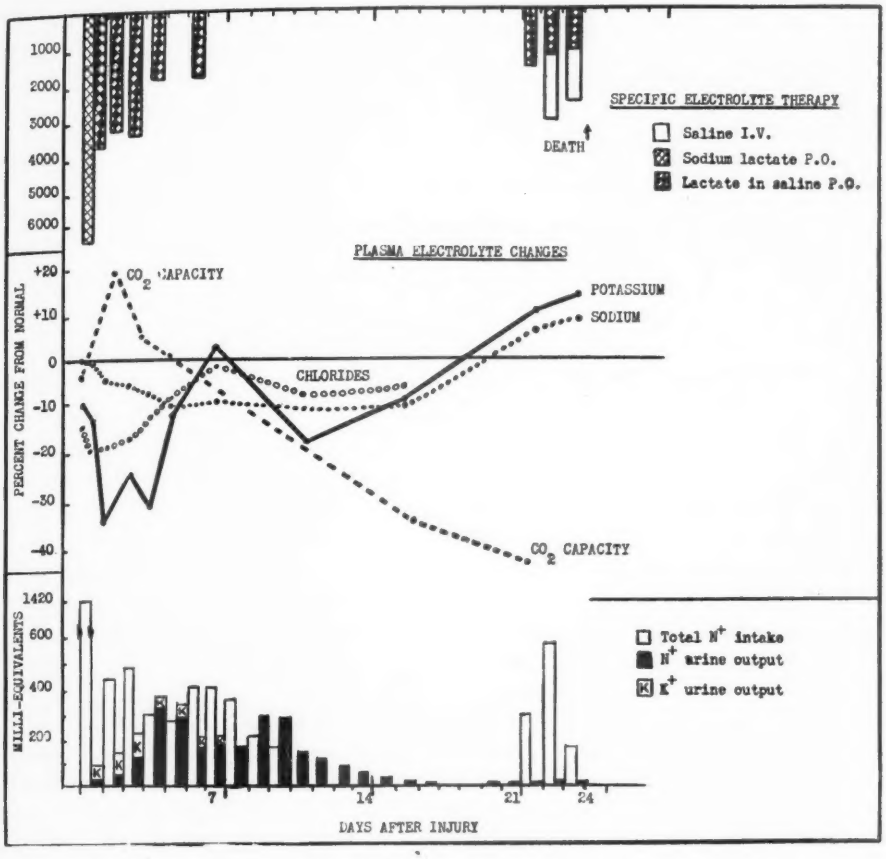


CHART VI-d.—Electrolyte intake, output and plasma changes in Case 6.

Case 6.—L. P., No. 729559 (Chart VI), a 29-year-old colored woman was admitted, December 13, 1943, approximately one hour after receiving a burn involving 44 per cent of her body surface. Her clothing had been ignited while she was fixing a stove. Treatment was managed by a combined group who agreed to give her oral electrolyte solutions *alone,* as advocated by Rosenthal and Fox. After a minimal cleansing the wounds were covered with an ointment gauze and pressure dressings. No intravenous therapy but nine liters of lactate and saline-lactate solution and two liters of other fluids were given orally during the first 24 hours. Urinary output during this time was 580 cc. and the patient vomited 4,300 cc. of fluid. Clinical signs of tetany were present on the following day but subsided after more saline and less lactate solution were given. Oral therapy alone was continued for two weeks with an average daily urinary output

of approximately two liters. Following the initial period of hemoconcentration there was a sharp fall in hematocrit and plasma protein levels to far below normal. Blood volume studies during this period were also subnormal by 20 to 40 per cent indicating that the actual anemia and hypoproteinemia was even greater than the deficits recorded on Chart V. Toward the end of the first week pulmonary complications developed which did not respond to sulfadiazine therapy. By the 14th day her condition appeared so critical it was felt that her only chance to survive lay in an effort to replace the protein and hemoglobin deficits by means of transfusions. In the next 11-day period 3,200 cc. of whole blood and 500 cc. of red cell suspension were transfused, with some improvement in her blood values. Additional lactate and saline were also given during the latter part of this period, but her general condition continued to grow worse and she expired on the 25th day of injury. In addition to the surface wounds the autopsy revealed pulmonary edema and congestion, bilateral hydrothorax, and partial atelectasis of both right and left lower lobes of the lungs.

COMMENT.—Oral lactate and saline solutions alone succeeded in sustaining this patient through the period of burn shock but left her with a *severe depletion of both hemoglobin and plasma proteins*. Some spontaneous recovery of the protein concentration was apparently accomplished by the mobilization of body reserves, but the anemia continued to get worse until transfusions were given. The difficulties of replacing such deficits once they are established have been mentioned by many other observers and it is generally agreed that it is much easier to prevent them or correct them by early transfusions. The forcing of electrolytes late in the course of this case, as in the previous case, was probably ill-advised in view of both the chemical and autopsy findings.

In contrast to the discouraging results obtained in the above two cases, the following four patients who suffered even more extensive burns are presented. They were given earlier and more intensive blood replacement with a successful outcome in each instance.

Case 7.—F. V. C., No. 757097 (Chart VII), a 27-year-old white chemist was admitted to the private pavilion, August 24, 1944, three days after suffering a flame burn involving 51 per cent of his body surface. While at work with some chemicals his clothing had been ignited and to extinguish the flames he had run across an open court to dive into a pond. The distribution of third-degree burns was almost identical to that in Case 6, but more extensive second-degree burns extended over most of his back. Shock therapy, given elsewhere, included the administration of 2,000 cc. of plasma during the first three days. After transfer to the Presbyterian Hospital blood studies showed he was still in a state of hemoconcentration, and an additional 1,600 cc. of plasma was transfused during the next three days. On the sixth day of injury his hematocrit was 25, indicating a severe deficit in red cell mass. During the next eight days he received a daily transfusion of whole blood or a total of 4,300 cc. for the eight-day period. After the sixth day of injury he took fluids and food by mouth extremely well, averaging over 200 grams of protein per day during the remainder of his hospital stay. Red cell concentration was kept within normal limits and his plasma proteins climbed steadily to normal and remained so. Healing progressed well and the third-degree areas were grafted on the 35th and 42nd days after injury, additional transfusions being given for operative support. Because of the shortage of donor sites "stamp" grafts were used except over the popliteal regions where full sheets of skin were placed. A good functional result was obtained, and the patient left the hospital walking three months and one week after injury.

COMMENT.—The conventional use of plasma in treating the shock phase of this case was successful but left him with a marked deficit in red cell mass. This was recognized early and enough blood to theoretically overcorrect the anemia was given. A quick return of appetite and progressive healing of the wounds followed.

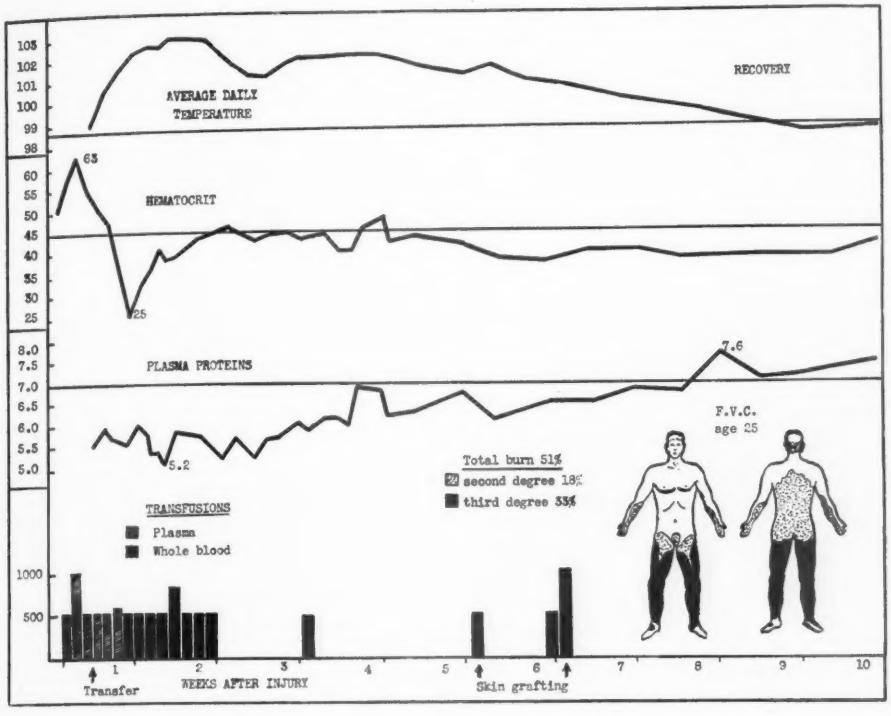


CHART VII.—Treatment and course of Case 7.

Case 8.—D. R., 644068 (Chart VIII-A), a 32-year-old elevator operator was burned on May 28, 1941, by an explosion of coal gas while lighting a furnace. He was admitted to the hospital 45 minutes later, with wounds involving 53 per cent of his body surface, largely second-degree in depth. Initial treatment included débridement of loose epidermis, application of a bland ointment dressing to the hands, forearms and face, and tannic acid-silver nitrate to the legs, buttocks and back. Replacement therapy consisted of 4,000 cc. of serum and 4,500 cc. of intravenous saline during the first 36 hours, with additional plasma and saline during the subsequent three days. By the sixth day a marked depletion in the hematocrit and plasma protein levels was apparent and whole blood transfusions were given daily for the next week and on alternate days for the following two weeks. The red cell and plasma protein deficits were soon corrected and the general course of the patient was satisfactory. Healing of the facial burns was complicated by an extensive infection of the left eye which necessitated evisceration on the 25th day. The tanned areas healed much slower than those treated with bland ointments and some skin grafting was necessary to aid healing in the scattered areas of full thickness loss. He left the hospital walking, four and one-half months after injury.

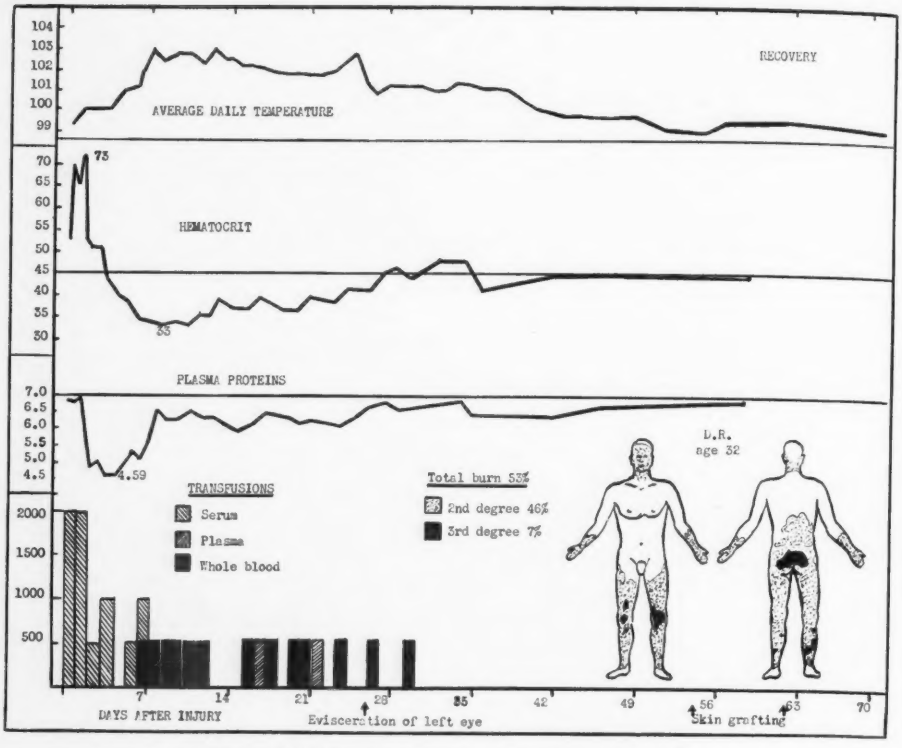


CHART VIII-a.—Treatment and course of Case 8.

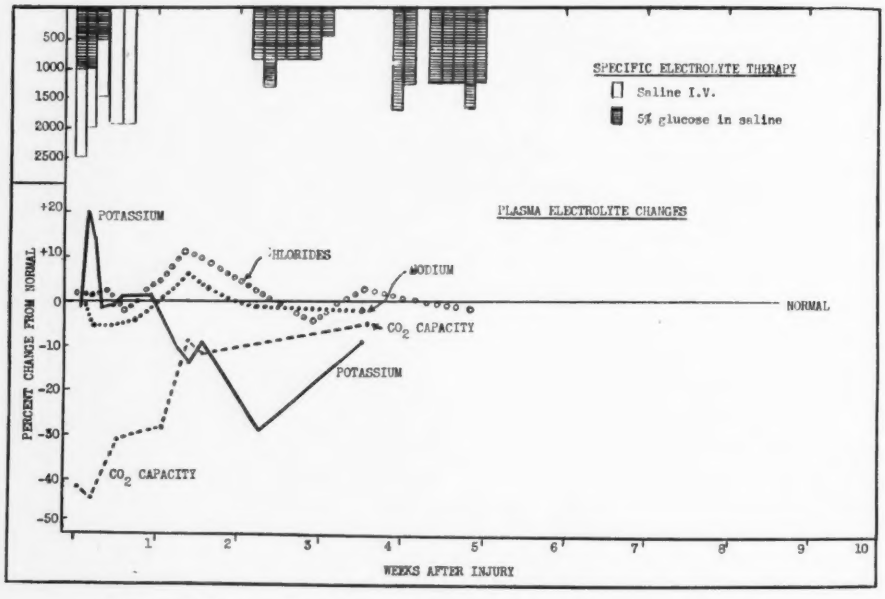


CHART VIII-b.—Electrolyte intake and plasma-changes in Case 8.

COMMENT.—The anemia of the post-shock phase was soon corrected in this case but might have been prevented had whole blood been given earlier. Also the acidosis of burn shock was slow in being corrected (Chart VIII-b) as compared with more recently treated cases given lactate solution (Chart XI). Local treatment with escharotics has since been abandoned by us because of the superior results obtained with pressure dressings and bland ointments.

Case 9.—J. N., No. 499757 (Chart IX), a nine-year-old colored girl who sustained a burn of 50 per cent of her body surface, January 24, 1944, when her clothing was ignited while she was lighting a candle at home. Early treatment, given elsewhere, con-

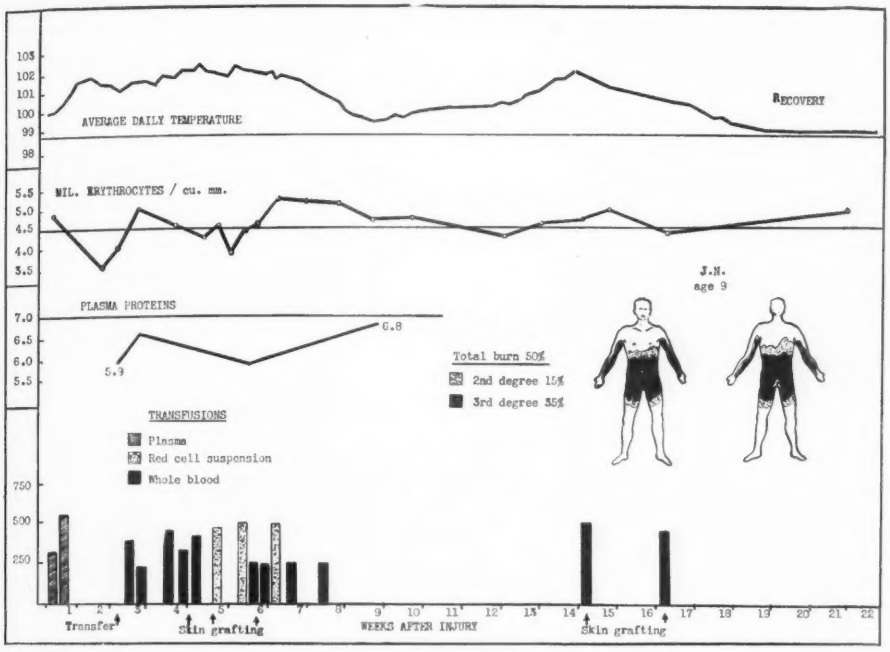


CHART IX.—Treatment and course of Case 9.

sisted of plasma and saline intravenously. The wounds were dressed with a variety of local applications. On February 9, 1944, 16 days after injury, she was transferred to our Plastic Surgery Service. Because of the demoralized state of the patient general anesthesia was used during dressings which were done at intervals of three to four days. A moderately severe anemia and hypoproteinemia were present upon admission and supportive therapy included frequent transfusions of whole blood and red cell suspensions totaling 4,550 cc. during the first month under our care, an amount equivalent to two and one-half times the normal circulating blood volume of the patient. Erythrocyte counts were maintained at a high normal during her most critical period. Within two weeks after transfer the slough had separated from the wounds and clean granulating surfaces were present (Fig. 6). Due to the magnitude of her wounds it was felt that autogenous skin grafting at this time might be too much for her to withstand. Accordingly, the patient's father was selected as a skin donor and eight dermatome sheets of skin (250 square inches) taken from him and used to cover the full-thickness

burn of her trunk and thighs. There was an immediate improvement in her appetite, morale and general appearance, anesthesia was no longer needed for dressings, and in the succeeding two weeks it was possible to apply autogenous grafts to both arms. With virtually all third-degree areas covered, the patient became nearly afebrile and was up and around the ward in a wheel chair. The secondary rise in her temperature noted between the 12th and 14th weeks (Chart IX) corresponded to the period of lysis of the homografts. By the time they had completely separated her arms and all second-degree wounds were fully healed and the total area remaining to be grafted was approximately half the size of her original wounds. She was in excellent condition to withstand the regrafting, which was done in two stages with the "stamp" graft technic, additional transfusions of whole blood being given for operative support. Fortunately, the patient did not develop keloids and a good functional result was obtained. She left the hospital walking, four and one-half months after admission.

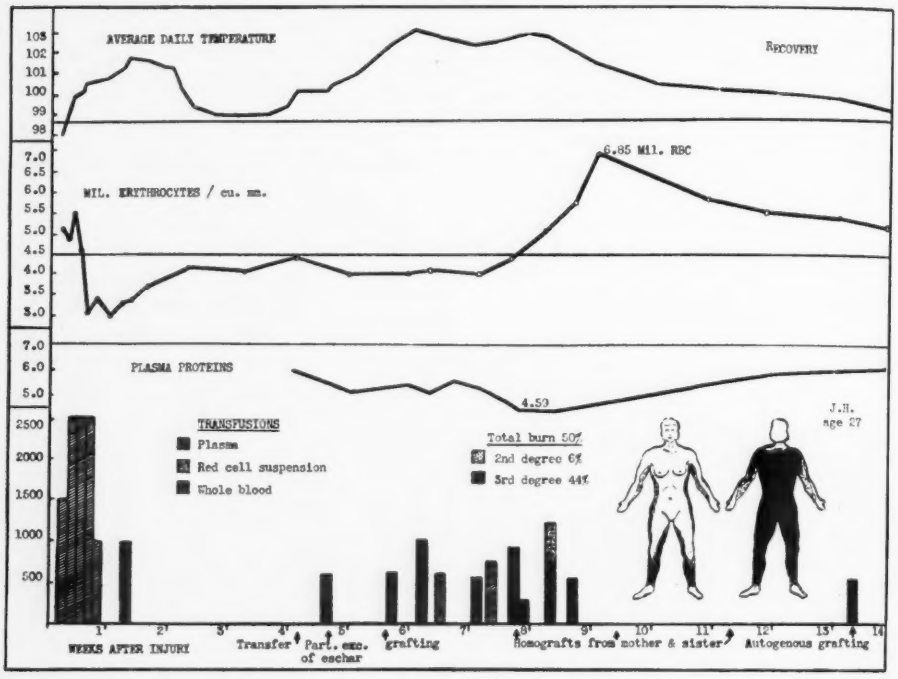


CHART X.—Treatment and course of Case 10.

COMMENT.—The liberal use of whole blood and red cell suspensions in this case was successful in maintaining both hemoglobin and plasma protein needs. Approximately one-half of her wounds were temporarily healed with homografts during the period when autogenous grafting and spontaneous healing were being accomplished in the remaining areas. Under this plan of treatment metabolic equilibrium was maintained through an extremely critical period.

Case 10.—J. H., No. 737446 (Chart X), a 27-year-old housewife who sustained a burn of 50 per cent of her body surface, January 22, 1944, when her dressing gown caught fire while she was tending her furnace. Initial therapy was carried out at a local hospital, where the wounds were treated with the triple-dye method. She re-

10 BURN CASES GIVEN LACTATE THERAPY ALONE OR IN ADDITION TO TRANSFUSIONS OF BLOOD AND PLASMA

15 BURN CASES SUPPORTED WITH EITHER ALBUMIN, BLOOD, PLASMA, SALT, OR SERUM, BUT WITHOUT LACTATE THERAPY

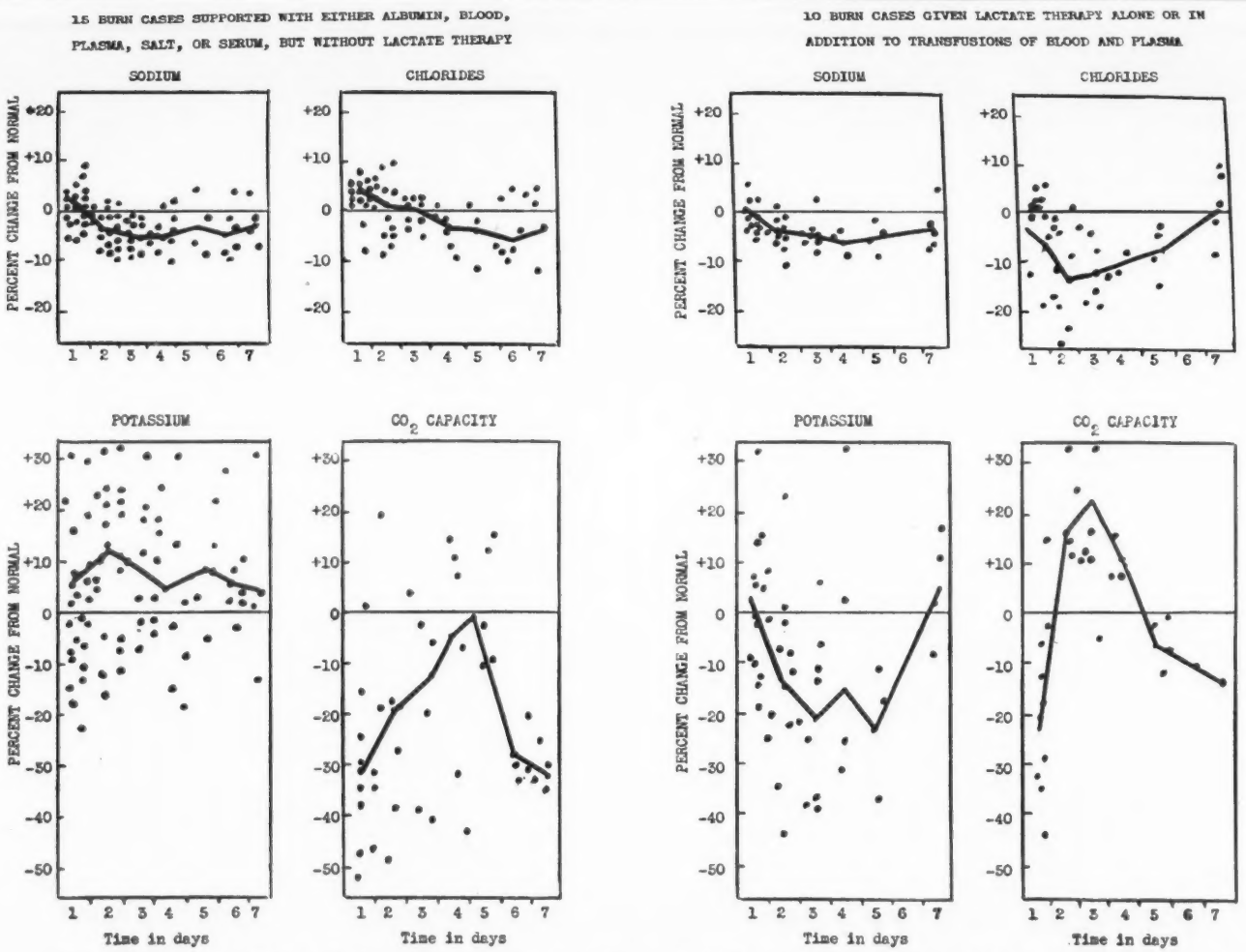


CHART XI.—The effect of sodium lactate therapy on plasma electrolytes in burns: The nonlactate treated group on the left shows slow elimination of excess potassium and inadequate correction of acidosis. The lactate-treated group on the right shows rapid decrease in potassium, overcorrection of acidosis and a tendency to hypochloremia.

ceived 10,000 cc. of plasma and 5,000 cc. of glucose intravenously during the first five days. Salt tablets totaling 10 Gm. daily and fluids, as tolerated, were given by mouth. On the sixth day her hemoglobin was 55 per cent and her erythrocyte count 3.0 million; 1,000 cc. of whole blood was then given and her erythrocyte count rose to 4.0 million. When transferred to the private service of Dr. Jerome P. Webster, one month after injury, she was in remarkably good condition. The triple-dye eschar was intact over the entire dorsal surface of her trunk and legs (Fig. 7), and there were no signs of infection beneath it. A portion of her arms which had been less deeply burned and had not received the eschar treatment were in the process of healing. Her blood studies at this time were at the lower limits of normal. On the fifth day after admission the eschar was surgically excised from the lower legs and part of the thighs. After a week on wet dressings, these areas were covered with autogenous "stamp" grafts which "took" satisfactorily. However, as other portions of the eschar became softened and undermined, the wound exudates increased in volume, her temperature rose, anorexia developed and wound-healing ceased. For a time it appeared her downward course could not be halted by the frequent transfusions of blood and plasma which were given. Still larger transfusions were used and when her outlook seemed hopeless she suddenly began to improve. Her erythrocyte count rose to 6.85 million, her temperature fell toward normal, appetite returned, wound exudates diminished, wound-healing was resumed and the nutritional edema which had developed in the hands, feet and labia disappeared. Her progress was slow but progressive. Homografts from the patient's mother and one sister (totaling 11 dermatome sheets of skin, Fig. 8) were used on the wounds until her general condition allowed further autogenous grafting which was carried out in three subsequent stages. A good functional result was obtained and the patient left the hospital walking, seven months after admission.

COMMENT.—Healing in this case was resumed only after an excess of red cells was supplied. It was of interest to note that the nutritional edema disappeared under this circumstance before there was a significant rise in plasma protein concentration.

THE RATIONALE FOR GIVING LARGE VOLUMES OF WHOLE BLOOD DURING THE HEALING STAGE OF SEVERE BURNS

The presence of anemia is of course a recognized indication for blood transfusions during the healing stage of burns, but when hypoproteinemia is more severe than the red cell deficit it is generally felt that plasma, albumin, amigens or amino-acid infusions are indicated. Our experience suggests that whole blood rather than blood substitutes is more effective in maintaining nitrogen balance, and we feel that a moderate excess in red cell mass may be indicated during the healing stage of severe burns. Several reasons why this should be true are suggested:

(1) When the viscosity of the blood is reduced by the depletion of plasma proteins a moderate excess in red cell mass will increase the viscosity of the blood and thereby contribute to more nearly normal hemodynamics.

(2) As a source of protein whole blood contains almost twice the concentration of an equal volume of plasma since the hemoglobin content represents roughly two and one-half times as much protein as the plasma content of whole blood. When a unit of blood is given its plasma component is immediately available to augment the plasma proteins or body reserves; its red cell mass,

if in excess of normal, represents a rich store of protein, virtually the only method known by which a protein store of significant size can be immediately supplied to an individual. The fact that hemoglobin protein can be converted to other body uses has been experimentally demonstrated by the work of Whipple, and his associates.[17]

(3) An excess in red cell mass may have an immediate sparing action on body proteins by displacing plasma volume and thereby reducing the amount of plasma protein needed to maintain circulation. Protein so spared may be used in wound-healing. That such a mechanism occurs is suggested by our recent experimental work[11] in which large volumes of whole blood were given rapidly to dogs. Although the total blood volume could be increased immediately as much as 50 per cent by giving a transfusion equal to 100 per cent of the circulating blood volume of the animal, the total blood volume would fall off rapidly to about 15 per cent above normal and then gradually to normal. The immediate adjustment was accomplished by a reduction in plasma volume to accommodate the excess red cell mass and as the excess of erythrocytes was gradually eliminated the plasma volume increased to its original level. There appears to be little danger of precipitating pulmonary edema by the administration of whole blood alone, as noted in our experiments and as recorded in somewhat similar studies in dogs made by Beck and Holman.[19] When saline was given with the transfusions however, pulmonary edema was encountered.

(4) Patients in our series in whom the anemia was quickly corrected, or overcorrected, assimilated much more protein given by mouth than those in whom the anemia was not controlled.

(5) The patient in the process of forming a large granulating surface may have a physiologic increase in his total blood volume to aid in the process of healing just as the pregnant woman enlarges her circulating blood volume to meet the demands of the gravid uterus. Since patients with extensive burns usually lose considerable weight, the increase in blood volume may be relative rather than absolute. Further blood volume studies in extensive burns are needed to expand our knowledge of the physiology of wound healing.

CONCLUSIONS

1. Replacement therapy in burn shock should be directed toward the restoration of all deficits in the circulating blood. These include red cells, plasma proteins, water and electrolytes. Whole blood transfusions fulfill these requirements more nearly than any other single agent.

2. Water and electrolytes can be administered to better advantage by mouth than by vein and will be absorbed in adequate amounts provided transfusions are also given. Sodium chloride solution in combination with lactate or bicarbonate is a more rational electrolyte mixture than sodium lactate solution alone in view of the tendency to alkalosis and hypochloremia which may result from vomiting and overalkalinization in burn shock.

3. The relative losses in plasma proteins and red cell mass may vary widely in different cases and are difficult to estimate during the period of hemoconcen-

tration unless blood volume determinations are available. In general, plasma losses will predominate in extensive second-degree burns while in third-degree burns the red cell mass lost from the circulation may equal or even exceed the losses in plasma volume.

4. If the anemia of the post-shock phase of a severe burn is not prevented by giving adequate amounts of whole blood in the shock period, it should be corrected as soon as it is recognized, for delay of even a few days may be disastrous.

5. During the healing phase of a severe burn whole blood should be administered in amounts adequate to theoretically overcorrect the anemia. If this is done the problem of maintaining nitrogen balance will be simplified.

6. In the presence of an anemia and hypoproteinemia uncontrolled electrolyte therapy by mouth or by vein is contraindicated since it will increase cellular edema and may lead to fatal pulmonary edema.

REFERENCES

[1] Abbott, W. E., Meyer, F. L., Hirshfeld, J. W., and Griffin, G. E.: Metabolic Alterations Following Thermal Burns. III. The Effect of Treatment with Whole Blood and an Electrolyte Solution or with Plasma Following an Experimental Burn. Surgery, **17**, 794–804, 1945.

[2] Abbott, W. E., Pilling, M. A., Griffin, G. E., Hirshfeld, J. W., and Meyer, F. L.: Metabolic Alterations Following Thermal Burns. V. The Use of Whole Blood and Electrolyte Solution in the Treatment of Burned Patients. ANNALS OF SURGERY, **122**, 678–692, 1945.

[3] Beck, C. S., and Holman, E.: The Physiological Response of the Circulatory System to Experimental Alterations. II. The Effect of Variations in Total Blood Volume. Jour. Exper. Med., **42**, 681–692, 1925.

[4] Brown, J. B., and McDowell, F.: Skin Grafting of Burns. Philadelphia, J. B. Lippincott Co., 1943.

[5] Duval, P., and Mourge-Molines: Physiologic pathologique et traitement des brûlures cutanées étendues récentes. Presse med., **45**, 1421–1424, 1937.

[6] Evans, E. I., and Bigger, I. A.: The Rationale of Whole Blood Therapy in Severe Burns. ANNALS OF SURGERY, **122**, 693–705, 1945.

[7] Fox, C. L., Jr.: Oral Sodium Lactate in the Treatment of Burn Shock. J. A. M. A., **124**, 207–212, 1944.

[8] Ham, A. W.: Histopathology of Burns. ANNALS OF SURGERY, **120**, 689–697, 1944.

[9] Harkins, H. N.: The Treatment of Burns. Baltimore, Charles C. Thomas, 1942.

[10] Lund, C. H., and Browder, N. C.: The Estimation of Areas of Burns. Surg., Gynec. and Obst., **79**, 352–358, 1944.

[11] McDonald, J. J., and Cadman, E. F.: The Tolerance of the Vascular System to Increases in Blood Volume. In preparation.

[12] Moyer, C. A., Coller, F. A., Iob, V., Vaughan, H. H., and Marty, D.: A Study of Interrelationship of Salt Solutions, Serum and Defibrinated Blood in the Treatment of Severely Scalded, Anesthetized Dogs. ANNALS OF SURGERY, **120**, 367–376, 1944.

[13] Moyer, C. A.: In discussion of above paper,[12] p. 403.

[14] Richards, D. W., Jr.: The Circulation in Traumatic Shock in Man. Bull. of N. Y. Acad. of Med., **20**, 363–393, 1944.

[15] Riehl, G.: Treatment of Severe Burns by Blood Transfusions. Wein. Klin. Wchnschr., **38**, 833–834, 1925.

[16] Robscheit-Robbins, F. S., Miller, L. I., and Whipple, G. H.: Hemoglobin and Plasma Protein. J. Exper. Med., **77**, 375–396, 1943.

17 Rosenthal, S. M.: Experimental Chemotherapy of Burns and Shock. III. Effects of Systemic Therapy on Early Mortality. Pub. Health Rep., **58,** 513–522, 1943.

18 Schievers, J.: Le volume sanguin apres brûlure étendue. Arch. int. de Pharm. et de Thérapie, **52,** 452–470, 1936.

19 Schjerning, Von: Über den Tod in Folge von Verbrennung und Verbruhung vom gerichtsarztlichen Standpunkte. Vrtljschr. f. gerichtl. Med., **41,** 24–66, 1884.

20 Scudder, J.: Shock: Blood Studies as a Guide to Therapy. Philadelphia, J. B. Lippincott Co., 1940.

21 Scudder, J., and Elliott, R. H. E.: Controlled Fluid Therapy in Burns. South. Med. & Surg., **104,** 651–658, 1942.

LESIONS OF THE MUSCULOTENDINOUS CUFF OF THE SHOULDER:

III. OBSERVATIONS ON THE PATHOLOGY, COURSE AND TREATMENT OF CALCIFIC DEPOSITS

HARRISON L. MCLAUGHLIN, M.D., C.M.
NEW YORK, N. Y.

FROM THE FRACTURE SERVICE OF THE PRESBYTERIAN HOSPITAL, NEW YORK, AND THE DEPARTMENT OF SURGERY, THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK, N. Y.

THE FRACTURE SERVICE of the Presbyterian Hospital, in New York, has been fortunate in having had the opportunity to study a great many painful shoulders during the past 15 years. Included were almost 2,000 lesions in which the symptoms centered around a calcific deposit to produce the condition commonly diagnosed and treated as "calcified subdeltoid bursitis." Codman[2] pointed out many years ago that the offending deposit is neither calcified nor, when it requires therapy, is it in the bursa. Widespread acceptance of the fallacy that the lesion is calcified and within the bursa, as well as the multitude of diverse treatments advocated for cure of the symptoms it sometimes produces, indicates clearly that this common condition is still poorly understood and frequently mistreated.

Almost all of the many forms of therapy, both logical and empirical, have been given an adequate trial in the course of the study. As a base-line for evaluation of the results there has been available a large series of cases which had no treatment other than sedation and palliation of pain. The long term follow-up has been somewhat less than adequate in many instances. However, the conclusions to be expressed concerning the immediate effect of various therapies are based upon adequate and critical clinical observations on the part of a trained personnel and embrace a large series of cases.

These conclusions may be stated very briefly. All adequately followed cases eventually recovered from their painful symptoms. This was true regardless of the type, presence or absence of treatment. The only variants included the character, severity and duration of pain and the occasional presence of certain general or local complicating factors resulting from the presence of a painful focus in the shoulder region. Certain treatments produced sure and speedy relief of symptoms within a time-period constant enough to allow of prognostication. Most treatments were accompanied, or followed by, relief at variable and inconstant periods following the inception of therapy. Upon analysis, the latter group were found to have a recovery rate quite comparable to that of the control cases who had no therapy other than sedation. In short, most of the therapies in common usage, while usually producing temporary amelioration of pain, had no appreciable effect upon the speed or completeness of the eventual recovery.

Gross, microscopic and bacteriologic studies of the condition have been possible in about 200 cases which were subjected to operation. This series included

cases in all stages of the condition, from the most mild to the most severe in degree. Operative findings correlated with pre- and postoperative clinical observations and, analyzed in comparison to the behavior of similar unexplored cases, have thrown considerable light upon the true nature and course of the condition. As a result it is now considered possible to reconstruct with reasonable certainty what might be termed the life cycle of the lesion and, *ipso facto,* a logical rationale for therapy.

ORIGIN

Codman maintained the lesion to be traumatic in origin with tendon degeneration and calcium deposition occurring as a secondary phenomenon. Meyer,[3] and others, hold degeneration to be the primary change, followed at times by secondary rupture of the degenerated fibers. There is some evidence to support the latter contention. Figure 1 shows degeneration of the tendon fibers of the supraspinatus, with minute diffuse deposition of calcium throughout the degenerated areas but no evidence of inflammation or rupture of the involved fibers. This section constitutes evidence that at least some degeneration and calcium deposition may occur without antecedent minute rupture of the tendon fibers. On the other hand, there is ample clinical evidence that trauma can activate painful symptoms around a previously quiescent or asymptomatic deposit. The onset of the clinical syndrome frequently follows within a few hours after a mild injury or over-use of the arm.

The earliest microscopic evidences of the lesion consist of hyaline degeneration in the collagen of the tendon fibers. The involved fibers soon become fibrillated and form what Codman called "straps" or loosened bands of fibers within the substance of the tendon. Motion of the part, aided by progression of the local degenerative change, further loosens these fibrillated strands, finally breaks them free from their attachments to the more normal surrounding tendon and curls them into rice-like bodies occupying a cavity within the substance of the tendon. Continued motion grinds these rice-like particles into a finely pulverized wen-like substance composed of necrotic tendon débris. Such a collection may or may not be characterized by the deposition of calcium salts in sufficient concentration so that an opaque shadow is produced on the roentgenogram. The shoulder from which the microscopic section illustrated in Figure 1 was taken showed no radiopaque shadow, and other nonopaque collections of tendon débris accidently encountered in the course of a tendon operation performed for some other condition, when subjected to chemical analyses, have shown a high concentration of calcium. It has been apparent, however, that almost all deposits productive of pain in the shoulder contain a sufficient concentration of calcium salts so that their presence and anatomic location become demonstrable by adequate roentgenologic studies of the part.

MECHANISM OF PAIN PRODUCTION

The predominant symptom associated with irritation by a calcific deposit

is pain in the shoulder region. It results from tissue tension at the site of an inflammatory reaction around the offending deposit. This inflammation is centered in and fairly well-restricted to the vascular peritendinous tissues rather than in the tendon tissues. The peritendinous structures associated with

FIG. 1.—High power view of section taken from supraspinatus tendon. X-ray showed no opaque shadow. Degeneration, loss of nuclei and deposition of cacium within the tendon fibers and no evidence of rupture or inflammatory change is present.

most round tendons consist of epitenon, or a tubular synovial sheath. That associated with the short rotator tendons of the shoulder consists of the synovial floor of the subdeltoid bursa. Therefore, while inflammation resulting from irritation by a calcific deposit may produce the clinical syndrome of tenosynovitis in tendons having tubular sheaths, it produces the syndrome of subdeltoid bursitis in the shoulder. The microscopic characteristics of the inflammatory reaction are not extraordinary except for the constant presence of giant cells, typical of tissue reaction to irritation by a foreign body. Bacteriologic investigations have failed to demonstrate the presence of aerobic, anaerobic or virus organisms. The deposit, composed of necrotic tendon débris, is a foreign protein and it, therefore, has seemed logical to

conclude that the inflammation is in fact a foreign body reaction to tissue irritation by its contents. This postulation provides the only logical explanation for certain peculiarities in the behavior of the lesion that, prior to increased knowledge resulting from operative examinations, were somewhat puzzling.

QUIESCENT OR ASYMPTOMATIC DEPOSITS

Calcific deposits in the shoulder are peculiar in that they are encountered roentgenologically in the complete absence of any past or present symptoms, almost as frequently as they are found accompanied by symptoms. Boardman Bosworth[1] found quiescent deposits in 165 of 6,061 normal shoulders. Two facts explain the quiescence of such lesions. The first is that the deposit originally forms in the tendon where it is enclosed within almost avascular tissues. The second is that the *sine qua non* for mobilization of an inflammatory reaction is adequate minute local circulation. Consequently, in the early stages while the deposit is surrounded by relatively avascular tendon tissue a minimal inflammatory reaction, if any, is possible.

Many asymptomatic lesions, discovered by roentgenograms taken for some other condition, have returned at a later date with pain due to irritation by the previously quiescent deposit. Probably most quiescent lesions eventually develop symptoms in some degree since the symptoms are nothing more than a subjective manifestation of nature's attempt to eradicate the lesion. It has been apparent that so long as the deposit remains buried in tendon it tends to remain quiescent, but that sooner, or later, it gradually or suddenly penetrates the overlying tendon fibers to come into contact with the floor of the subdeltoid bursa, following which an inflammatory reaction immediately is mobilized with ensuing symptoms.

VARIATION OF SYMPTOMS IN LESIONS APPEARING IDENTICAL BY ROENTGENOLOGY

Operative findings have demonstrated that the degree of inflammation varies in accordance with the quantity of irritant material in contact with the bursal floor. This explains another previously puzzling peculiarity of the lesion, *i.e.*, the great variation in severity of pain accompanying deposits that seem of identical size by roentgenogram. There is no relation between the size of the deposit and the severity of the symptoms to be expected. The explanation rests in the fact that symptoms vary as the amount of material actively irritating the bursal floor rather than the total quantity of the material as judged by the size of the deposit.

It has been found that mild or intermittent chronic symptoms are to be expected when a few particles of the deposit penetrate the tendon and come into contact with well-vascularized peritendinous tissue. Such symptoms may subside if the amount of irritant is small enough to be absorbed and eliminated by phagocytosis, only to recur upon penetration of the tendon by additional material from the buried deposit.

Acutely painful lesions are found to have a major portion of the deposit in

contact with the bursal floor. Release of a large portion of the material from the depths of the tendon cavity may result from degeneration and final spontaneous rupture of the tendon fibers overlying the deposit. Such is the mechanism for production of acute attacks that commence without known cause. The softened overlying tendon fibers also may be ruptured by a minor wrench or overuse of the arm, as attested by the high incidence of acute attacks that come on a few hours after some minor injury or strain. Minute traumatic factors of this type may be overlooked but are of considerable importance for the establishment of compensability when the syndrome occurs in connection with occupation.

There is little difference between any two acute incidents from a clinical viewpoint. It has been demonstrated beyond doubt, however, that the location of the deposit is of some importance in determining the character of the symptoms during the chronic stages of the condition. Prior to the increased knowledge, made available by operative investigations, it was difficult to understand why two apparently identical lesions should produce, on the one hand, a constant ache, and, on the other, nothing more than acute catches of pain in the shoulder on certain motions. Deposits in the subscapularis tendon often remain quiescent until, or unless, an acute attack supervenes. Those in the supraspinatus or anterior portion of the infraspinatus tend to produce a constant ache aggravated by motion. Those in the posterior portion of the infraspinatus, or the teres minor, are characterized by sharp catches of pain on certain motions such as putting the arm into a coat sleeve and are apt to remain asymptomatic at other times. Exploration under local anesthesia has demonstrated that pain constantly is accentuated by any increased tension in the tendon containing the deposit and markedly aggravated by compression of the inflamed tissues around the deposit against the acromion or the anterior edge of the coraco-acromial ligament. It is, therefore, only logical that a deposit in the supraspinatus portion of the cuff where it is under constant tension by gravity and crushed against the acromion on almost every glenohumeral motion should produce more severe and constant chronic symptoms than one in the anterior or posterior portion of the cuff where gravity plays a relatively unimportant rôle and where impingement against the acromion is possible only in certain extremes of position.

VARIATIONS IN LOCAL PATHOLOGY

The consistency of the material within the deposit and the tension under which it is enclosed within the tendon cavity constitutes two constant differences between the acute and the chronic lesion. The deposit productive of chronic symptoms invariably is dry, cheesy or wen-like, and infiltrated through tendon tissue within a relatively poorly circumscribed cavity under little or no tension. The deposit productive of acute pain is always wet, greasy, and the consistency of tooth paste or heavy cream. In addition, the acute lesion always is under distinct tension within a rather well-defined cavity from which the material is apt to spurt upon incision. This change in the consistency and ten-

sion of the lesion results from infiltration and dilution of the dry chronic or quiescent deposit by inflammatory exudate as irritation progresses. Both the relative consistency and tension of the lesion may be determined by interpretation of the roentgenograms. The chronic lesion is roentgenologically manifested by a rather dense shadow with an ill-defined or irregular periphery, whereas the acutely inflamed deposit is represented by a well-defined globular and frequently flocculent shadow of relatively less opacity. Evaluation and determination of both the consistency and tension of the deposit as well as the exact anatomic location is of some therapeutic import as will be illustrated by the results of certain needling procedures.

NORMAL COURSE OF THE LESION IF UNTREATED

Chronic stages of the condition may persist over a lengthly interval. The study includes patients with a history of more or less constant mild pain for as long as 15 years. A great many patients, first seen because of mild and chronic symptoms, subsequently returned for treatment of a superimposed acute attack. A considerable percentage of the patients suffering from an acute episode gave a history of antecedent minor symptoms. These facts, in conjunction with the rarity of the lesion in the anatomy laboratory where unselected cadavers exceed 66 years of age, indicate that most, if not all, deposits are eliminated by some spontaneous mechanism prior to the sixth decade and tend to confirm the conviction arrived at from operative investigations that this mechanism consists of the inflammatory phenomena under discussion.

It seems probable that intermittent attacks of mild or moderate pain represent a mechanism for gradual depletion and eventual elimination of the deposit by repeated inflammatory responses of minor degree, each of which phagocytizes a small amount of the irritant material. It has been demonstrated, conclusively, that the acute episode also represents a spontaneous mechanism for eradication of the lesion. In direct proportion to increasing severity of the symptoms there occurs an increased degree of inflammation around the deposit. The enclosed material becomes diluted by exudate and the lesion presents as a tense, furuncle-like swelling in the bursal floor. The subsequent train of events somewhat simulates that of a furuncle. Tension increases until rupture occurs, following which the contents of the deposit are discharged into the synovia-lined cavity of the bursa and absorbed. As soon as rupture takes place the intense throbbing pain characteristic of the acute stage commences to subside. Within a few days not only do the symptoms disappear, but so also does the roentgenologic evidence of the deposit. Operative findings have shown that the tendon cavity fills-in by granulation with eventual fibrous tissue replacement of the residual defect.

The self-limiting character of the condition makes the prognosis for eventual recovery from any one attack reasonably certain. Multiple deposits in the same shoulder seldom produce symptoms simultaneously and such a condition is the usual cause of recurrent acute episodes. The unknown factors in

the prognosis of a single lesion include only the severity and duration of the symptoms to be expected. Consequently, the therapeutic problem concerns not the question of recovery as much as the time of recovery and the control of pain during symptomatic stages of the condition.

THERAPY

No therapy designed to combat a calcific lesion is warranted except in the presence of symptoms which on clinical and roentgenologic examination are with reasonable certainty the result of irritation by the deposit. Pain in the upper extremity may emanate from many sources and the incidental presence of a calcific deposit in the shoulder region may result in a waste of valuable time and effort and allow the true etiologic agent to progress needlessly if therapy is administered on the basis of roentgenologic evidence alone. Several malignant lesions of the upper humerus, a number of herniated cervical disks, and a considerable number of coronary lesions have been encountered which gave a history of protracted and useless treatment designed to combat the effects of harmless, incidental calcific deposits in the shoulder prior to recognition of the true cause of pain.

Following determination that the deposit is the cause of pain therapy may be indicated for one of two reasons. It may be required as a palliative measure for the reduction and control of pain during the symptomatic period accompanying the spontaneous eradication of the irritating focus. It may be required as a curative agent by reason of symptoms, the duration or severity of which warrant more than palliative treatment from the patient's point of view. No therapy is warranted by the presence of a deposit, *per se*, unless, or until, the lesion produces pain. Analysis of the results following the many forms of therapy that have been evaluated during the course of this study leads to the conclusion that the only curative therapies available are those designed to simulate nature's method of cure, *i.e.*, eradication of the offending deposit. All others are chiefly palliative in effect and their professed curative powers, when examined in the light of the known self-limiting nature of the local pathology and compared to adequate controls, have been disproved or found to be purely empirical in nature. Radiation therapy, the exact mechanism and effect of which is still incompletely understood, appears to occupy an intermediate therapeutic status in the light of present knowledge. It has proved of frequent but inconstant value in providing speedy relief of pain in the acute cases. In the chronic cases it has proved of negligible value and is worthy of mention only for emphasis of its potential dangers. It is in the chronic case that the temptation to give just a little more therapy is most prevalent and catastrophic burns may result. Only two curative measures have been proved by an adequate series of recoveries which took place within a constant time-period.

1. NEEDLING PROCEDURES

Various types of needling procedures have been practised. The only one productive of constant, speedy, and permanent relief of symptoms was that

which evolved from an understanding of the local pathology as described above and which undertook to insert the needle into the cavity containing the irritant material and deflate the tension within the cavity by puncture and aspiration of its contents. Even this procedure proved of uncertain value in the treatment of chronic lesions. The dry material characteristic of the chronic lesion can be aspirated only with difficulty and after surgical dilution by injecting into it a sufficient quantity of saline so that the resultant mixture becomes semifluid enough to go through a needle. This can be done only in a few selected cases and the over-all results following attempts to aspirate a considerable number of chronic lesions was disappointing enough so that the practice has been discontinued. Puncture alone is sufficient to produce immediate reduction of pain in the acute case and complete subsidence of pain within the next few days. Aspiration of some of the contents of the acutely inflamed deposit is considered advisable, not from a curative standpoint, but because recovery of the material from the deposit constitutes evidence that the aim of the procedure, puncture of the tense cavity, has been accomplished. Such a procedure guarantees the patient suffering from an acutely inflamed deposit immediate relief of the intense throbbing pain and progressive subsidence of any residual ache so that complete and permanent recovery occurs within a few days. Other needling procedures such as regional infiltration with novacaine, multiple perforations of the bursa, and irrigation of the bursal cavity have been followed by frequent but inconstant relief of pain in acute cases.

The general trend of clinical evidence indicates that any agent or procedure which temporarily eliminates pain and allows motion of the arm may indirectly result in rupture of the tense acutely inflamed deposit if it is in a location where it becomes pinched on motion of the shoulder. For this reason many therapeutic procedures may be followed by a considerable percentage of cures even though they are employed as a routine rather than as a method for the accomplishment of a specific purpose, arrived at through logical rationale.

2. OPERATIVE REMOVAL OF THE DEPOSIT

Almost 200 cases have been explored and had the deposit or deposits removed. This method of treatment produces the most certain and permanent results. It has been necessary in less than ten per cent of all cases, and the great majority of operated cases were done as a procedure of choice on the part of the patient. Only twice has operative removal been considered imperative. Both cases were in acute pain which seriously jeopardized the status of a coincident condition; one, a pneumonia and the other, a precarious pregnancy. Both deposits, although acutely inflamed, were not amenable to aspiration and operative removal was carried out under local anesthesia. The incidence of recurrent attacks of acute pain due to multiple deposits has been high enough to warrant consideration of operation as an advisable procedure when more than one deposit is found in an acutely inflamed shoulder. Otherwise the most tenable indication for operation is present in the chronic

condition productive of symptoms sufficiently protracted or severe to warrant it from the patient's point of view. Preoperative localization of the lesion and adequate placement of the surgical approach makes the procedure a minor one. An incision more than three centimeters in length is rarely necessary. No postoperative restriction of motion or use is necessary or wise and the total hospitalization required seldom exceeds three days.

CHOICE OF TREATMENT

The study has resulted in the evolution of a simple clinical philosophy based upon an increased understanding of the lesion. The immediate problem usually demands a decision between curative and purely palliative therapy. Seldom is anyone but the patient qualified to make such a decision. After a full explanation of all aspects of the situation he is asked to decide whether he can carry on comfortably with appropriate help in controlling the symptoms and with a reasonably certain expectation of eventual spontaneous recovery, or whether the symptoms warrant more radical curative therapy in an effort to eliminate them quickly and permanently.

The chronic condition warranting curative therapy deserves operative removal of the deposit as the only certain and speedy method of obtaining permanent relief.

The chronic condition warranting nothing more than palliation may be treated by any combination of sedative measures that are convenient and that result in reduction of pain. Therapy that fails to do this is not worth while. Simple home measures including heat, aspirin and a program designed to prevent disuse and stiffness of the arm have been found to be as efficient as all types of formal therapy.

The acute condition warrants curative therapy. The treatment of choice is puncture of the tense deposit and aspiration of its contents by needle under local anesthesia. Palliation usually is necessary during the next few days. Multiple deposits in the acutely inflamed shoulder and certain other selected acute cases warrant operative intervention.

REFERENCES

[1] Bosworth, B. M.: Calcium Deposits in the Shoulder and Subacromial Bursitis. Journal of the American Medical Association, **116**, 2477–2482, May 31, 1941.

[2] Codman, E. A.: The Shoulder. Thomas Todd Co., Boston, 1934.

[3] Meyer, A. W.: Use Destruction in the Human Body. California and Western Medicine, **47**, No. 6, December, 1937.

MASSIVE PANCREATIC HEMORRHAGE*

CASE REPORT

RICHARD H. MEADE, JR., M.D.
CHICAGO, ILL.

CASES of acute hemorrhagic pancreatitis in which recovery has occurred have been reported in increasing numbers in recent years. Many of the recoveries have been in patients upon whom no operation was performed. Accordingly, the more certain recognition of the lesion by means of blood amylase studies has made many surgeons feel that operation should not be undertaken when a definite diagnosis can be made with any degree of confidence. However, in the minds of most physicians there is still present a belief that most of the severe cases will die regardless of the form of treatment. Because of this impression it seems worth while to record a case in which, at operation, the pancreas seemed to be replaced by a massive hematoma and yet the patient recovered and has remained well for eight years. No report of a similar case has been found since the paper of F. W. Draper,[1] a medical examiner in Boston, was published in 1886.

Case Report.—The patient, a white male, age 55, was admitted to the Episcopal Hospital, in Philadelphia, at 11 P.M., December 5, 1937, complaining of severe pain in the upper part of his abdomen. At 10 A.M. that morning he had noticed a heavy feeling in his epigastrium and a short while later vomited several times. This was followed by the appearance of severe pain in the upper abdomen which in two hours failed to be affected by the administration of morphine. He grew progressively worse in spite of ingesting a large number of pills given for the relief of his pain.

For the past two years he had been working as a machinist. For several months he had been treated by his doctor for a vague type of indigestion. He had never smoked and drank only sparingly. Two years previously he had injured his pelvis in an automobile accident but had no persisting disability.

Physical Examination.—Upon his admission to the hospital, he was seen to be a frail, sick-looking man, apparently suffering from severe abdominal pain. There was no apparent jaundice or cyanosis, and he showed no evidence of dehydration. Temperature 96.4°F.; pulse 80, respirations 20. The peripheral blood vessels showed thickening of their walls. The chest was normal and the heart sounds were regular and of fair quality, without murmurs. Blood pressure 122/80. The area of liver dullness started at the sixth rib in front and was diminished in the axilla. The abdominal wall was retracted and showed no appreciable movement on respiration. There was diffuse tenderness and muscle spasm but the most marked tenderness was in the left upper quadrant and in the left flank. Peristalsis was not audible. Rectal examination revealed fullness high up anteriorly and tenderness in the same area. White blood cell count 16,000, with 94 per cent polymorphonuclears, of which half were unsegmented forms. The urine showed traces of albumen and of acetone, and hyaline casts, but no sugar. A diagnosis of acute hemorrhagic pancreatitis was thought to be more suitable than one of acute perforation of a gastric or duodenal ulcer and operation decided upon. He was given morphine sulphate

* This case was originally presented at the combined meeting of the New York Surgical Society and the Philadelphia Academy of Surgery, in Philadelphia, February 14, 1940.

and scopolamine and an intravenous infusion of 5 per cent glucose in normal salt solution, 250 cc., before going to the operating room.

Operation.—Spinal anesthesia with pontocaine (0.11 Gm. in 3 cc. of 10 per cent glucose solution) preceded by the subcutaneous injection of ephedrine sulphate (.050 Gm.) 20 minutes before. A right subcostal incision was made and practically no bleeding was encountered even when the rectus muscle was cut across. The blood pressure was then found to be 44, and epinephrine was injected subcutaneously and an intravenous infusion of 10 per cent glucose in normal salt solution started. There was immediate improvement, and the operation was continued without any further difficulty. On incising the peritoneum there was an escape of dark blood. The peritoneal surfaces appeared normal, there was no fat necrosis and no exudate. In the base of the transverse mesocolon dark blood could be seen, and in the region of the pancreas could be felt, a firm mass about eight times the normal size of that organ. On incising the peritoneum over the head of the pancreas the mass was found to be a large hematoma but no active bleeding could be demonstrated. The liver was somewhat pale but the spleen and other organs appeared to be normal. Although the gallbladder showed no evidence of disease and was not distended a cholecystostomy was performed to allow for the fullest decompression of the biliary tract. The gallbladder bile was black and liquid. A catheter, with fenestrations, was inserted and held in place by two purse-string sutures. Omentum was wrapped around the tube which was brought out through the wound. The abdominal wall was closed with interrupted through-and-through sutures of silkworm gut. At the end of the operation the patient's condition was fair.

The next morning his condition was quite good, and from then on he made a slow but progressive recovery with a marked temporary disturbance of his sugar metabolism and with attacks of pain in the region of his pancreas.

Subsequent Course.—During the first few days he had suction drainage of his stomach maintained and fluids were given intravenously. On the first day after operation his blood sugar was found to be 322 mg. per cent and he had sugar in his urine. His urinary amylase was also found to be slightly elevated this first day. After that one unit of insulin was given with every 2.5 Gm. of glucose given intravenously and a diabetic regimen inaugurated. By the fifth day the blood sugar had fallen to 148 mg. per cent. From this date onward the blood sugar fell and did not rise again except on one occasion. His diet was gradually increased and the insulin regulated. By the time of his discharge from the hospital, February 20, 1938, he was tolerating a diet of 2,500 calories without insulin and without spilling any sugar into his urine. Two glucose tolerance tests were done, with evidence of considerable improvement in the one of February 15.

His wound healed by primary intention except for the drainage tract. Bile drained in small amounts and varied in quality. When it was thin and watery he had no discomfort. When it became dark and thick, as it did at times, he had a dull pain in the region of the pancreas. Several small flat calculi were passed from the drainage tract on the 27th day after operation, but within 18 days after this all drainage had stopped.

He had several attacks of pain in the region of the pancreas, associated with sweating and with a drop in blood pressure. The worst one occurred on Christmas morning, 20 days after operation, and was so severe that it was thought he might die. However, following the administration of epinephrine, and of glucose intravenously he promptly recovered, but for a week thereafter ran fever and for another week he had a variously-sized mass in the region of the pancreas, which was quite tender. This mass was thought to be due to a necrosis of the pancreas but its disappearance within two weeks without the subsequent discharge of any necrotic material from his drainage tract seemed to rule out this possibility.

His blood pressure, except during the attacks of supposed hypoglycemic shock, seemed to vary inversely with his asthenia. During the first six days when he seemed prostrated the pressure varied between 130/70 and 140/78, with only two recordings

lower than this, and the pressure was determined every four hours. As he improved and felt stronger the blood pressure fell to a lower level and ranged between 90/62 and 120/70, with the average about 100/70.

Following discharge from the hospital he was examined at frequent intervals for the next two years. He regained his strength slowly, but had no other symptoms. His fasting blood sugar was consistently normal and he showed no sugar in his urine, although on a liberal diet without candy or similar sweets. In January and February,

TABLE I

SUMMARY OF LABORATORY STUDIES*

Bacteriologic:
Peritoneal fluid at time of operation. Culture—no growth.
Bile obtained from gallbladder at operation. Culture—Bacilli (identification of the Bacilli was not made).

Chemical Studies:
Bile from gallbladder at operation—bile salts and chloride normal.
Urinary amylase 1st day after operation—slightly increased. 4 weeks later—normal.
Two years after operation:
Blood amylase (colorimetric test) Feb. 1940—Normal
Blood lipase Feb. 1940—Normal

Blood Wassermann and Kahn: Dec. 6, 1937—Negative.

Blood Sugar—Dec. 6, 1937	322 mg.%	
7,	250	
8,	218	CO_2 57.9 vol. %
10,	250	
11,	148	
12,	127	CO_2 66.3
13,	148	48
14,	120	
15,	107	
16,	118	

After January 5, 1938 it never was above 110.

Glucose Tolerance Tests
(100 Gm. glucose given)

	Blood Sugar Readings					Urinary Sugar Readings				
Date	Fasting	After 30 Min.	After 60 Min.	After 2 Hrs.	After 3 Hrs.	Fasting	30 Min.	60 Min.	2 Hrs.	3 Hrs.
Feb. 2, 1938	86 mg. %	190	262	252	208	Neg.	Neg.	Neg.	1%	1%
Feb. 15, 1938	93	123	212			Neg.	Neg.	Neg.		
Mar. 29, 1938	101	147	308	344		Neg.	No spec.	Neg.	No spec.	
Jan. 30, 1940	89	117	254	172	226	Neg.	Neg.			

Liver Function Tests
February 1940

Hippuric acid 2.6 Gm. Bromsulphalein—18 min. 3% retention, 30, 60 min.—none.
Cholecystogram—Gallbladder filled well but only half emptied contents after fatty meal.

* The chemical studies on the bile were done by Dr. Cecelia Riegel, and the amylase and lipase determinations by Dr. Daniel Dozzi, in the Laboratory of Research Surgery of the University of Pennsylvania.

1940, studies of his liver function by means of the hippuric acid excretion test and bromsulphalein excretion showed no evidence of impairment. Blood amalyse and blood lipase studies were also normal. A cholecystogram, in February, 1940, showed normal filling of the gallbladder, but it only half emptied after the fatty meal. He has continued to work and lead a normal life, without symptoms, but has had to follow a diet to keep his blood sugar within normal limits. During 1945 his blood sugar varied between 107 mg. per cent in April to 176 in December (Table I).

COMMENT.—This then was a case in which a considerable part of the pancreas was involved in an hemorrhagic process which did not produce any apparent fat necrosis or peritonitis. No source for the hemorrhage could be found, and the diffuse involvement of the organ seems strong evidence against a vascular accident. The severe diabetes which was present immediately following the operation would indicate a considerable suppression of the pancreatic islet activity. No material which resembled necrotic tissue ever escaped from the drainage tract. Furthermore, the diabetes gradually became less and less severe so that on his discharge from the hospital the only evidence of it was seen in the glucose tolerance test. This demonstrates the reversibility of the process but its true nature is not apparent.

Whether the operative intervention was of value, or not, cannot be definitely stated. Although the diagnosis of acute hemorrhagic pancreatitis was considered before operation there was also considerable support for the diagnosis of acute perforation of a duodenal or gastric ulcer. No blood amylase study was made, but even had it been done and had shown evidence of pancreatic damage it would have been felt that an exploratory operation was still necessary.

The value of cholecystostomy is also problematic. There was no evidence of biliary tract disease at the time of the operation, or from a study of the bile removed from the gallbladder, but the passage of a small stone through the drainage tract following an attack of colicky pain suggests that there was some disease present. Certainly, there was no evidence of back pressure in the gallbladder.

It would seem logical to conclude that this patient recovered from a severe hemorrhagic lesion of his pancreas in spite of operative intervention.

SUMMARY

The case is reported of a 55-year-old male patient, who was found, at operation, in 1937, to have a massive hemorrhage diffusely involving his pancreas. Following cholecystostomy he recovered, after evidence of severe diabetes during the first month. During the eight years since his operation he has been leading a normal life without symptoms but has had to regulate his diet to maintain his blood sugar at a normal level. The cause of the hemorrhagic process was not discovered but the damage to the pancreas was sufficient to cause severe diabetes during the early postoperative period and permanent, but slight, disturbance of the islet activity since then. The only justification for operation was the uncertainty as to the diagnosis. There is no definite evidence that it was responsible for the patient's recovery. This report has been made because of the rarity of this condition, its severity, and the fact that the patient recovered and has remained well for eight years.

I am indebted to Dr. John Davis Paul for a report on the condition of this patient in recent years.

REFERENCE

[1] Draper, F. W.: Trans. Assn. Am. Physic., 1, 243, 1886.

WAR INJURIES OF THE CHEST

LT. COL. RICHMOND L. MOORE, M.C., A.U.S.

FROM THE SURGICAL SERVICE, HALLORAN GENERAL HOSPITAL, STATEN ISLAND, NEW YORK.

STATISTICS, recently reported by Carter and DeBakey,[1] indicate that chest wounds comprise from one-fourth to one-third of all battle casualties and about one-twelfth of the wounds of soldiers that survive admission to medical units. The high incidence and seriousness of these conditions have made their treatment a matter of great importance. The Army has been fully cognizant of this and has endeavored to place surgeons with special training and experience in thoracic surgery in all of our Theaters of Operation. That this was done with wisdom has been proved by the relatively low mortality rate for chest injuries in the present war, as compared with all previous wars.[1]

The reports of Carter and DeBakey, and others, covering the incidence, types, complications, treatment, and mortality of chest wounds in the present war have been of great interest and help to the men working in this field. The purpose of this paper is to review the subject with special emphasis on treatment and the physiologic alterations which accompany the pathology of these wounds.

The proper treatment of thoracic wounds demands that the physiologic alterations which accompany them be well understood. These may be due to any of the following conditions: (1) Open pneumothorax, usually associated with "sucking wounds" of the chest wall; (2) tension pneumothorax; (3) surgical emphysema, either superficial or mediastinal; and (4) cardiac tamponade. All, or any, of these may be associated with a chest injury. Therefore, it is most essential that they be kept in mind when a patient with a chest wound is first examined. All of them may be serious and if overlooked may lead to deaths which could have been prevented. The initial treatment of thoracic injuries consists mainly in combatting shock, the proper care of the wound and correcting these physiologic disturbances.

PATHOLOGY

Open Pneumothorax.—The dangers of an open pneumothorax have been well understood for many years. The high mortality which followed early open drainage in the streptococcal empyemas of the last war was later proved to be due to the ill effects of the open pneumothorax that was produced by operation. When this method of treatment was changed and the pleural fluid in the early cases was evacuated by repeated aspirations, rather than by open drainage, the mortality fell from about 50 per cent to about five per cent. Graham and Bell,[2,3] in a series of experiments on animals, showed that the harmful effects of an open pneumothorax are due to pulmonary collapse which, in turn, leads to a decrease in vital capacity, asphyxia and death. Graham and Bell also showed that in the presence of a mobile mediastinum, the effects of

an open pneumothorax are bilateral and that the degree to which the vital capacity is reduced is directly related to the size of the opening in the chest wall. One of the fundamental principles in the treatment of empyema, namely, not to institute open drainage in the early or acute stages of the disease is based on these experiments. When a hole is torn in the chest wall by a shell fragment or bullet, the effect is exactly the same as establishing open drainage in the early or acute stages of an empyema. Air is sucked in through the opening with each inspiration. The intrapleural pressure rises and the expansion of the lung is reduced. In order to compensate, the patient breathes faster and with greater effort, and this, in turn, rapidly leads to exhaustion. Open wounds of this kind, so-called "sucking wounds," should be closed as soon as possible. Experience has shown, however, that closure by suture is inadvisable unless all of the necessary surgery has been completed. When the existing facilities are inadequate for this, or trained personnel is not available, treatment, in general, should be limited to first-aid measures; namely, control of shock, control of hemorrhage, excision of devitalized and soiled tissue, and removal of readily accessible foreign bodies. The wound is then covered with a pad of vaselined gauze. This is either sutured to the skin, or strapped in position with adhesive plaster.[4] In most instances this method will suffice until the soldier can be delivered to a suitable hospital for definitive operating. The vaselined pad is effective not only in preventing the entrance of air into the chest, but also in permitting the escape of air and fluids from the chest. This is an advantage, because, otherwise, serious respiratory embarrassment might result from a tension pneumothorax or an accumulation of blood.

The effects of crushing injuries of the chest which are accompanied by multiple rib fractures may be exactly the same as those of an open pneumothorax. In these cases the reduced pulmonary expansion is due to paradoxic motion of the chest wall at the site of the injury. The more the chest wall is sucked in during inspiration, the less the lung is sucked out and the greater the decrease in vital capacity. Here, again, the patient compensates by breathing faster and with more effort. Treatment of these injuries should be directed toward stabilization of the mobile areas of the chest wall and this is best accomplished by adhesive strapping.

The effects of an open pneumothorax on the circulation are less spectacular, but animal experiments have shown a rise in venous pressure and a decrease in cardiac output. These changes have been attributed to the reduced intrathoracic sucking effect which helps to draw blood to the heart and also to a direct tamponade effect on the heart itself.

Tension Pneumothorax: When a lung is pierced or torn, or, more rarely, when a bronchus is lacerated, air may repeatedly be sucked into the pleural cavity during inspiration and trapped. The opening, acting as a ball-valve, allows the air to get in, but does not allow it to get out. Under these conditions, the intrapleural pressure steadily increases and the resulting tamponade effect may reach alarming proportions and seriously interfere with both pul-

monary expansion and the filling of the right side of the heart. This leads to severe dyspnea and, in extreme instances, to acute circulatory failure, evidenced by a falling systemic pressure, a high venous pressure, a weak, rapid pulse, pallor and sweating. In civil practice, this condition, which is known as a tension pneumothorax, is occasionally seen after pneumonectomy or lobectomy, when the closure of a bronchial stump or lung is insecure or gives way in the presence of infection. It may also follow rupture of an emphysematous bulla. It is more likely to be due to laceration of the lung or bronchi by fragments of broken ribs. The immediate treatment is very simple: The pressure can be relieved quickly by introducing a needle through one of the intercostal spaces. A simple method is to use a needle with a flange, which can be readily strapped to the chest wall. If such a needle is not available, a flange can be improvised by using an ordinary cork.[4] The needle is inserted through the cork, which, in turn, is fixed to the chest wall with adhesive strapping. The second intercostal space in the midclavicular line is a convenient location for introducing the needle. If left in position the needle should be connected with a "water-seal."

Surgical Emphysema.—Surgical emphysema is of two types, namely, superficial and mediastinal. The superficial variety may result from laceration of the lung by in-driven rib fragments or penetration of the lung by a missile. In either case air escapes into the subcutaneous tissues, either directly from the lung at the site of an adhesion, or indirectly through the medium of an interposed pneumothorax. From the chest wall the air may spread upward to involve the tissues of the neck and face, or downward to the abdominal wall. In extreme instances, even the extremities are involved. The diagnosis is readily established by the crackling sensation which one gets on palpating the involved areas and the air in the tissues is easily recognized on roentgenograms. Fortunately, the condition in itself rarely demands any special treatment because the opening in the pleura usually becomes sealed after a short period of time and the air in the tissues is readily absorbed. If the pleural opening does not close, however, and the condition becomes progressive and causes symptoms, relief should be obtained by introducing a needle into the pleural space for the escape of the air. The recognition of a superficial emphysema is important because it may be an indication of a tension pneumothorax.

Mediastinal emphysema is a much more serious condition because air escaping into the mediastinum does not find a ready outlet and there is serious danger of compression of the great vessels, and even the esophagus. Here the air escapes from a lacerated trachea or large bronchus and tends to spread towards the neck. The condition is readily recognized from a soft swelling in the suprasternal notch and the diagnosis can be confirmed roentgenographically. Radical treatment is indicated only when the symptoms of compression are severe enough to endanger life. Treatment is directed toward relief of pressure. In some instances this can be easily accomplished simply by incising the swelling in the neck. In exceptional instances, a thoracotomy may be

necessary, followed by incision of the mediastinal pleura and suture of the lacerated bronchus or trachea.

Cardiac Tamponade.—Cardiac tamponade is a term which is commonly used to refer to acute cardiac compression caused by the rapid accumulation of blood or exudate within the pericardial sac. Since the pericardium is a dense, fibrous, relatively inelastic membrane, it is not distended appreciably by an acute increase in pressure. Observations have shown that from 200 to 250 cc. of fluid in a normal pericardium is a sufficient amount to cause circulatory failure. The pressure of the fluid obstructs the filling of the heart and the blood is dammed-up in the great venous reservoirs of the body. Should the intrapericardial pressure equal the effective venous pressure, the blood can no longer enter the right auricle and death follows. The clinical picture is that of circulatory failure, characterized by a low systemic pressure; a high venous pressure, distant or absent heart sounds; an imperceptible or thready pulse, pallor and diaphoresis. Roentgenograms show a large cardiopericardial shadow with sharply defined edges and fluoroscopic examination reveals a diminution or absence of the normal cardiac pulsations. In chest injuries, the syndrome is caused by intrapericardial bleeding which usually results from a stab wound in the front of the chest to the left of the sternum, in the third or fourth interspace. The source of the bleeding is most likely to be the right ventricle or the anterior descending branch of the left coronary artery. The right auricle, right coronary artery and the intrapericardial portions of the great vessels (all of which lie behind the sternum) are less likely to be damaged.

The treatment of this condition demands the greatest haste. The indications are two: first, and foremost, to relieve the pressure; and, second, to stop the bleeding. The time required for roentgenologic and fluoroscopic examinations might mean the difference between life and death. These examinations, therefore, should be omitted, unless the condition of the patient is obviously such as to permit their being undertaken without danger. Preparation for operation and transfusion should be made at once. Experiments on dogs and preliminary observations on patients, recently reported by Cooper, Stead, and Warren,[5] indicate that the preoperative administration of intravenous fluids is beneficial. If the patient's condition is stationary or improving, one or more pericardial taps might suffice. On the contrary, if the evidence of this is lacking or questionable, it is much safer to expose the pericardium at once, evacuate the blood, and attempt to locate the source of the hemorrhage and control it by suture. When there has been serious loss of blood, one or more transfusions should then be given.

Hemothorax: Hemothorax is a very frequent complication of thoracic wounds. According to Davies and Cooper,[6] it occurs in 70 per cent of all chest injuries in modern warfare. It also frequently occurs following crushing injuries of the chest with simple rib fractures and almost always accompanies penetrating wounds. The bleeding may be from the lung itself, but more often comes from the chest wall, and can usually be traced to lacerations

of the intercostal vessels. In World War I the incidence of infection of hemothorax complicating penetrating wounds of the chest was about 25 per cent.[7]

The treatment of hemothorax has been a subject of much discussion. Some have advocated extreme conservation, aspirating only to relieve pressure or pain. Others have advocated aspiration with air replacement and still others, aspiration alone. The latter method, namely, aspiration alone, with a view toward emptying the pleura as quickly and completely as possible, is now widely approved as the treatment of choice. The points that have been made against the conservative treatment of a hemothorax are the following: (1) Blood is a good culture medium and encourages the development of infection and empyema; (2) blood may not be completely absorbed and this, in turn, leads to the development of a so-called fibrothorax with contraction and fixation of both the chest wall and lung; and (3) in war injuries, infection and incomplete absorption of an hemothorax are not uncommon complications, probably because of the great amount of tissue damage that so frequently accompanies the injury.

The injection of air after aspiration is now condemned as being both unnecessary and harmful. The procedure apparently originated with the thought that by keeping the lung collapsed recurrence of bleeding after aspiration would be avoided. This idea is based on the assumption that the source of bleeding is pulmonary, whereas it is now well-known that in the great majority of instances at least the source of bleeding is the chest wall. The method also overlooks the fact that bleeding from the lung tends to cease spontaneously because of the low pressure in the pulmonary circuit. That the method is harmful has been demonstrated by experience accumulated in the present war. Case analyses have shown that the incidence of chronic hemothorax and chronic empyema is higher in patients with hemothorax treated by aspiration and air replacement than in those treated by aspiration alone.

When an hemothorax can not be controlled by aspiration because of clotting, the proper treatment is an early thoracotomy with evacuation of the blood clot. When this is not done the surface of the compressed lung is soon covered by a layer of fibrin, which, in turn, becomes organized and fixes the lung in its compressed state. When this condition exists the treatment should include, in addition to evacuation of the clot, excision of the thickened membrane which prevents the lung from reëxpanding. The membrane is more easily excised in the early stages of an hemothorax. Later, after an interval of two to three months, it becomes more intimately attached to the lung and the plane of cleavage is more difficult to develop. Good exposure for operating, hemostasis, early reëxpansion of the lung and obliteration of the pleural space are of great importance. When satisfactory hemostasis is not obtained it is probably advisable to establish closed, catheter drainage, rather than depend on aspirations, for evacuation of the blood. Otherwise clotting may recur and a second thoracotomy become necessary.

The treatment of chronic hemothorax by excising the fibrous membrane covering the underlying lung appears to have reduced the incidence of chronic

empyema in the present war. Case 1 (Fig. 1) is an example of a satisfactory result. Case 2 is an example of a postoperative, or recurrent, "chronic" hemothorax, for which a second thoracotomy and decortication were necessary. Figure 2 is an example of a chronic hemothorax with areas of calcification in the thickened membrane on the lung.

TREATMENT OF VARIOUS TYPES OF WOUNDS

Chest cases should have a high priority among battle casualties and taken as quickly as possible to an installation with complete anesthesia and operative facilities, preferably one with personnel experienced in thoracic surgery. Endotracheal anesthesia should be routine in all intrathoracic procedures, and facilities for suction should be at hand. The wounds should not be sutured until all of the surgery, necessary at the time, has been completed. Suturing then should be directed primarily toward closing the pleura. When it is necessary to approximate muscle and fascial layers of the chest wall these structures should be sutured loosely. The skin and subcutaneous tissues should be left open. If the wounds are sutured without thorough débridement, or in the presence of extensive lung damage, infection of the chest wall and pleura is very likely to develop. If the wound is a "sucking" one, a pad of vaselined gauze, which is either sutured to the skin, or strapped in position with adhesive plaster, will prevent the aspiration of air and at the same time permit drainage while the patient is being transported. An accompanying hemothorax should be evacuated as completely as possible with a view toward obtaining early reëxpansion of the lung and obliteration of the pleural space. If there is a delay and infection is already established when the casualty reaches a suitable installation the primary operation should be restricted as far as possible to simple procedures, such as the removal of readily accessible foreign bodies and incisions to maintain drainage of the chest wall and pleura.

Wounds of the Chest Wall: The treatment of wounds of the chest wall does not differ from the treatment of similar wounds in other parts of the body. The adjacent skin surface should be cleansed; readily accessible foreign bodies removed; bleeding controlled and all devitalized tissues excised. After this, the wound should be left open, with or without the local administration of one of the sulfonamides. Secondary suture should be done later (after four days) if the condition of the wound permits.

Perforating Wounds: The treatment of through-and-through bullet wounds of the chest, which cause slight pulmonary damage and do not injure large blood vessels or other important structures, consists mainly of the treatment of hemothorax. The treatment of hemothorax is discussed under a separate heading. It is well-known that wounds of this type, which are commonly seen in civil life following attempts at suicide, do well. The same is true of similar wounds incurred in combat. When a bullet is deflected from its course by impact with a rib, however, the damage to a lung and to the chest wall at the site of exit may be extensive. Extensive destruction

of tissue may be caused also by shell fragments. Case 3 illustrates some of the complications which may follow a wound of this type.

Penetrating Wounds with Retained Foreign Bodies: The common types of retained foreign bodies which have been seen in the present war are shell fragments, bullets, pieces of clothing and splinters of bone. In treating these injuries the risk of the operative procedure which would be required for removal of the foreign body has to be balanced against the risk of complications which are likely to develop if the foreign body is left in place. Experience has shown that pieces of clothing and fragments of bone are especially likely to lead to serious infection and every effort should be made to remove these. On the contrary, metallic foreign bodies are well tolerated. Nevertheless, it is felt that these should be removed also when they are large (diameter of 2 cm. or more), causing symptoms, free in the pleural space with hemothorax, or, because of their position, considered to be a threat to vital structures such as the heart, esophagus, and large blood vessels. It is generally agreed that unless there is immediate danger of serious complications only those foreign bodies that are readily accessible should be removed at the initial operation, preferably done as soon as possible after the injury is received. Timing of a secondary operation, for removal of foreign bodies which are not disturbed at the initial operation, but which are removed later because of their size or position, is of great importance. It is considered safer to postpone the secondary operation for at least two weeks, and in many instances longer, to allow the patient time to recover completely from the loss of blood and the acute effects of trauma. Cases 4, 5 and 6 are presented as examples of penetrating wounds of the chest with retained foreign bodies.

Thoraco-abdominal Wounds: Whenever a missile penetrates the thoracic cavity the possibility of its having traversed the diaphragm and entered the abdomen must always be borne in mind. This is particularly important if the thoracic wound is low, in the region of the diaphragm. Roentgenograms of the abdomen as well as the chest should regularly be taken. When operation is being planned, careful consideration should be given to all the facts relative to both the thoracic and abdominal wounds. There is no standard procedure that can be applied in all cases. Certain general principles, however, do apply: (1) Endotracheal anesthesia is vitally important in cases of this kind; (2) the hemothorax which is almost certain to be present, should be aspirated before operation; (3) a celiotomy should always be done and the incision should be large enough to permit examination of all of the abdominal viscera; (4) "sucking wounds" of the chest must be closed early in order to save life, and in most instances take priority over the abdominal exploration; (5) the possibility of a diaphragmatic hernia must be considered; and (6) a foreign body suspected of being embedded in the liver may be more easily reached by a transthoracic approach which is extended through the diaphragm than by a celiotomy. Case 7 is an example of a thoraco-abdominal wound.

Infected War Wounds of the Chest: The treatment of infected war wounds of the chest may be briefly summarized as follows: (1) Pleural and

pulmonary suppuration are forestalled by early operation (within six to ten hours), removal of foreign bodies, local and systemic use of the sulfonamides or penicillin, and leaving the superficial layers of the wound in the chest wall open; (2) infected hemothorax in the early stages is properly treated by aspiration. Thoracotomy with rib resection (open drainage) should be postponed until the pleural exudate is definitely purulent. This allows time for localization of the pleural infection, avoids the dangers of an open pneumothorax, and reduces the risk of a large or a total empyema; and (3) pulmonary or pleuropulmonary suppuration secondary to retained foreign body should first be treated by drainage. Extensive operative procedures for the removal of foreign bodies should be avoided in the presence of active infection. Lobectomy in wounds of this type when indicated should be postponed, if possible, until the infection is brought under control.

CASE REPORTS

Case 1.—A commander of a tank company was wounded in action, July 12, 1944, sustaining a penetrating shell fragment wound of the left chest, with fracture of the eighth rib. Treatment overseas consisted of débridement and closure of the wound on the day of injury and two thoracenteses. When the patient arrived at the Halloran General Hospital, September 1, 1944, roentgenograms of the chest showed an encapsulated hemothorax on the left and a shell fragment overlying the 7th intercostal space near the vertebral column. Operation, October 30, revealed a cavity containing 150 cc. of old blood clot, and a rigid, fibrous membrane covering the adjacent part of the lung. Operation consisted of evacuating the blood clot and excising the membrane, following which the lung was reëxpanded and the wound closed without drainage. Roentgenograms of chest on the 15th postoperative day showed complete reëxpansion of the lung. Removal of the shell fragment was not advised.

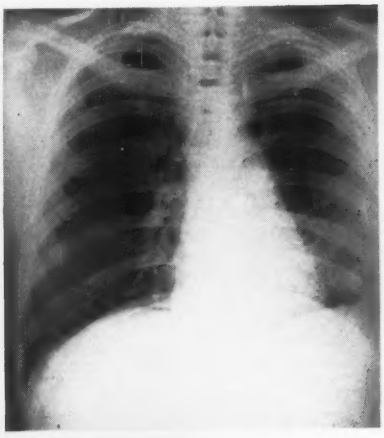
COMMENT: This case illustrates the successful treatment of a small, chronic hemothorax by decortication of the lung (Fig. 1).

Case 2.—This soldier sustained a perforating shell fragment wound of the chest, March 29, 1945, the fragment lodging in the soft tissues of the back at the level of the second lumbar vertebra. An effort to aspirate a complicating hemothorax was not made until April. When the soldier came under our care, in June, examination showed contraction and marked limitation in motion of the right side of the chest. Roentgenograms showed an encapsulated hemopneumothorax in the right axilla. Operation was delayed by an attack of malaria until July 21, 1945. Exploration on this date revealed a cavity of approximately 300 cc. and, as in Case 1, the underlying lung was covered by a rigid, fibrous membrane. This was excised and, after inflating the lung, the wound was closed without drainage. The postoperative course was complicated by a second hemothorax which could not be controlled by aspiration because of clotting. Consequently, the chest was reopened on August 13, 1945, and after evacuating the blood clot the lung was decorticated a second time. Following this operation the wound was not sutured, but closed temporarily with a silk and gauze tampon which was left in place for seven days. It was considered safer not to suture the wound after the second operation because of the danger of infecton. The cavity finally closed on December 1, 1945.

COMMENT: The initial operation on this soldier was unsuccessful because the blood which accumulated in the pleura later clotted and could not be removed by aspiration. The danger of this complication is always present

1-A

1-B



1-C

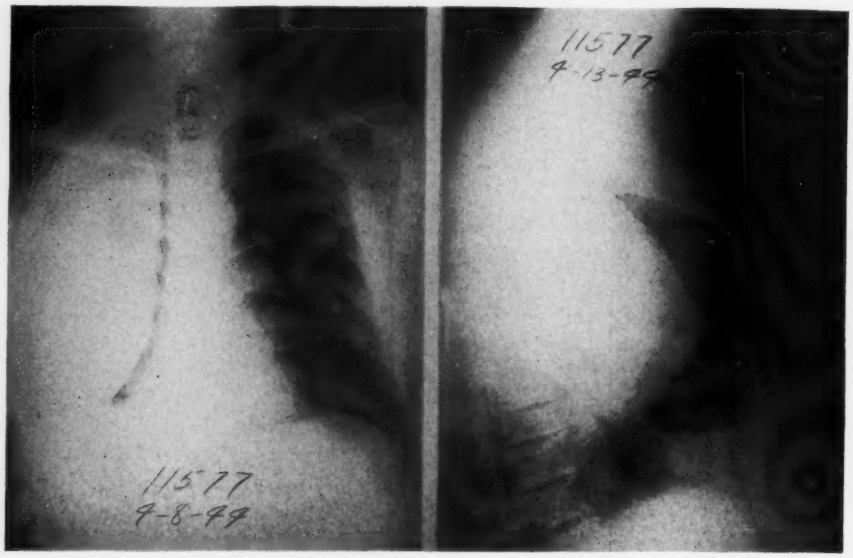
FIG. 1.—Case 1: (A) Roentgenogram of chest showing encapsulated hemothorax on the left and metallic fragment in the 7th left intercostal space near the vertebral column.

(B) Roentgenogram of chest 15 days after evacuation of blood clot and decortication of the lung. Lung completely reëxpanded.

(C) Photograph of patient on the 15th postoperative day, showing primary healing of the wound.

after a decortication of the lung, and when postoperative oozing is profuse and hard to control, it is perhaps safer to establish and maintain some form of closed drainage until the lung has reëxpanded and closed the pleural space.

Case 3.—A 24-year-old soldier was struck by a machine gun bullet on September 22, 1944. The bullet entered the left chest posteriorly between the scapula and spine and emerged anteriorly in the midclavicular line, about two inches below the clavicle, lacerating the lung and shattering the posterior portion of the fourth rib and the anterior portions of the second and third ribs. Both wounds were sutured about 30 minutes after



2-A 2-B

FIG. 2.—(A) Roentgenogram of chest showing a large, encapsulated hemothorax on the right side with areas of calcification in the thickened membrane on the surface of the lung. This was an unexpected finding in a soldier who was evacuated from the Aleutians in the Spring of 1944. He gave no history of an injury to his chest but stated that he had been knocked down by an automobile on August 31, 1941. No roentgenograms of the chest were taken at that time. This soldier refused operation.

(B) Lateral view of the same patient.

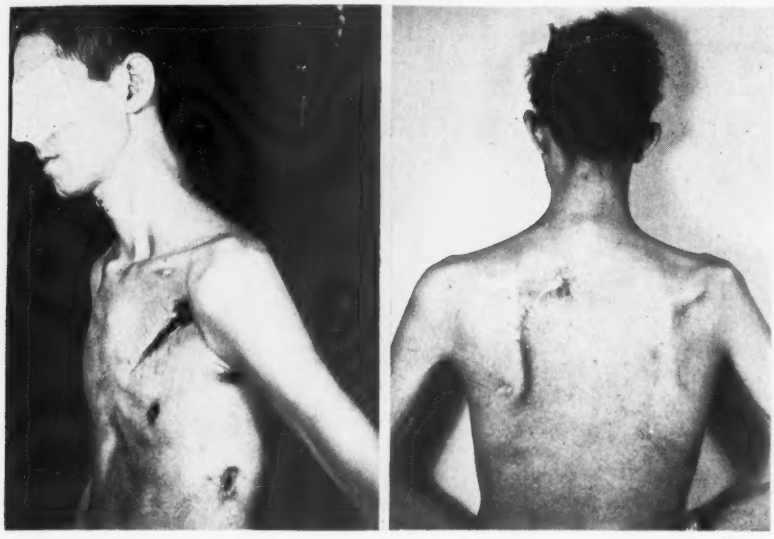
injury. On the following day both wounds were reopened, the lung was sutured and, after débridement, the wounds were closed a second time. Subsequent to this the anterior wound became badly infected and the soldier developed a left empyema. On admission to the Halloran General Hospital, in December, he had lost 38 pounds. The left chest was markedly contracted and fixed. The anterior wound was still draining and through the opening in the chest wall one could see a large defect in the lung with multiple fistulae. A drainage tube entered a residual empyema cavity at the site of a previous rib resection. This soldier had not been assigned to our hospital for definitive care and, in accordance with Army procedure, had to be transferred to another institution (Fig. 3).

Case 4.—A 21-year-old soldier was struck in the right chest by a machine gun bullet on July 28, 1943. The wound healed satisfactorily, and a complicating hemothorax cleared without aspiration. After this the soldier had no symptoms referable to his chest until June, 1944, when he coughed up a small amount of bright red blood. The hemoptysis

recurred in September. Roentgenograms of the chest showed a 25-caliber bullet situated posteriorly on the right side at the level of the tenth intercostal space. Films made after the instillation of lipiodal showed no evidence of bronchiectasis. The bullet was removed on October 13, 1943. The space which it occupied communicated freely with the bronchial tree and contained a small amount of necrotic material, culture of which revealed an *hemolytic Staphylococcus aureus*. Convalescence was satisfactory except for a small empyema which healed rapidly after rib resection and drainage.

COMMENT: This case demonstrates that a foreign body (in this particular instance, a machine gun bullet) may be embedded in a lung for many months before causing symptoms. The history suggests that the hemoptysis was secondary to infection due to the *hemolytic Staphylococcus aureus* (Fig. 4).

Case 5.—A soldier received multiple penetrating wounds of the left chest on July 28, 1944. On July 30, 1944, all wounds were débrided and readily accessible foreign bodies were removed. The soldier arrived at Halloran General Hospital, October 9, 1944, with



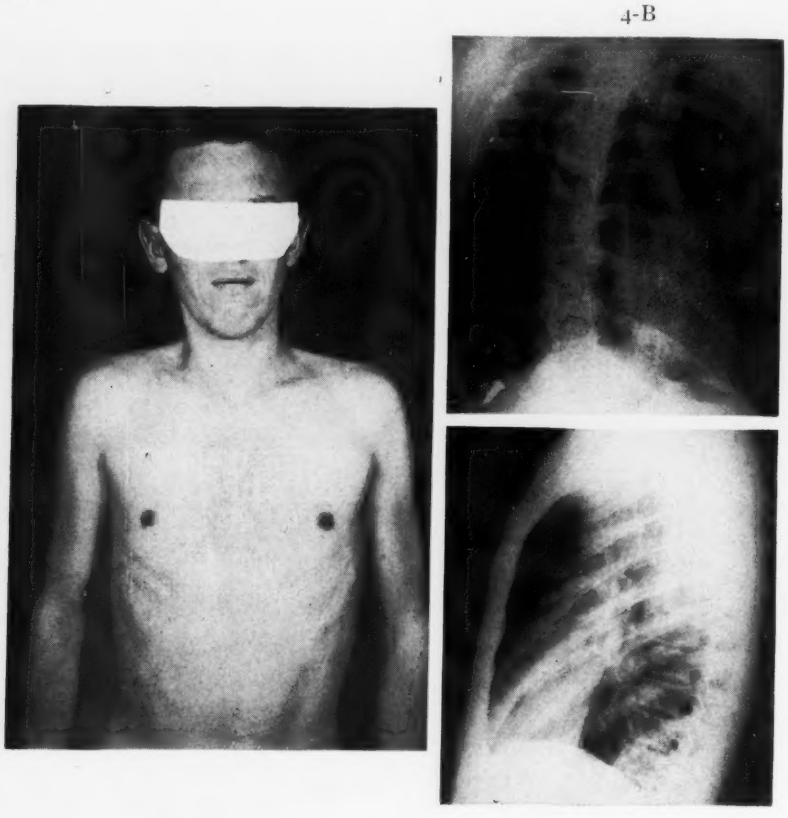
3-A 3-B

FIG. 3.—Case 3: (A) Photograph made on January 25, 1945, showing the extreme degree of malnutrition and the contraction of the left chest. The anterior wound below the left clavicle represents the point of exit of the bullet. The wound in the axilla is the site of the rib resection which was done on October 10, 1944, and leads into the dependent part of the empyema cavity.

(B) Photograph showing the wound in the left scapular region, point of entrance of the bullet. This wound was completely healed when the patient came under our care on December 27, 1944. Note the scoliosis secondary to the contraction and fixation of the left chest.

a temperature of 103° F., pulse 120, and respirations 30. He was pale and weak and showed evidence of considerable weight loss. R.B.C. 2,270,000; W.B.C. 3,900, and Hb. (Sahli) 7.5 Gm. Roentgenograms of the chest showed a metallic fragment, measuring about 2 x 3 cm., in the posterior portion of the left lung at the level of the tenth dorsal vertebra. The patient received penicillin, repeated blood transfusions and vitamin therapy. A subcutaneous abscess in the left scapular region was drained, October 19, 1944, and in

addition to 25 cc. of purulent material three pieces of woolen shirt were evacuated. Culture of the exudate showed *B. coli* and *nonhemolytic Staphylococcus aureus.* After this the temperature quickly dropped to normal and convalescence was satisfactory except for an attack of malaria which responded quickly to atabrin. By the middle of November the patient had gained 19 pounds. R.B.C. 4,870,000; W.B.C. 5,850, and Hb. 14.5 Gm. The time was considered opportune for removal of the metallic fragment in the left lung, but inasmuch as the soldier had now become transportable and had not been assigned to this hospital for definitive care, he had to be reported to the Registrar for transfer to another institution.



4-A 4-B 4-C

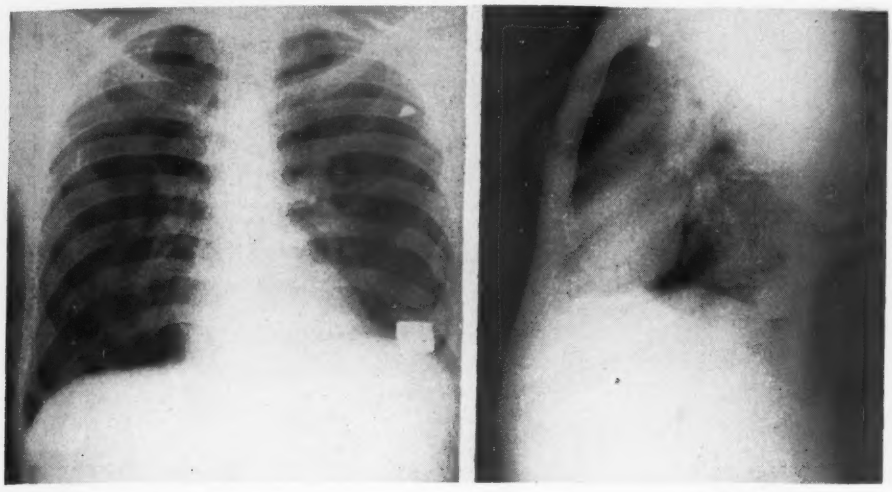
FIG. 4.—Case 4: (A) Photograph of the patient taken after admission to the Halloran General Hospital, showing the scar at the point of entrance of the bullet.

(B) Roentgenogram made on October 4, 1944, in the left anterior oblique position, showing the bullet in the right chest lying opposite the 10th intercostal space.

(C) Lateral roentgenogram showing the bullet to be situated posteriorly just above the dome of the diaphragm.

COMMENT: This case is another example of a metallic foreign body being retained within the lung for many months without causing symptoms. Furthermore, it shows the ineffectiveness of penicillin in controlling a suppurative process in the presence of tissue damage, foreign bodies and a nonsusceptible organism (Fig. 5).

Case 6.—This patient was struck by a shell fragment, November 7, 1944, sustaining a penetrating wound in the right supraclavicular region. He recovered rapidly from the effects of his injury and felt well within a short time. When he came under our care in May, 1945, he was in excellent condition and had no complaints. Roentgenograms of the chest showed the shell fragment in the right upper lobe and an healed fracture of the right second rib. The shell fragment was removed in September, 1945, and cultures taken from the cavity which it occupied showed *nonhemolytic Streptococcus* and *nonhemolytic Staphylococcus aureus*. Penicillin was given postoperatively. Convalescence was uneventful except for a small pleural effusion which cleared without aspiration.



5-A 5-B

FIG. 5.—Case 5: (A) Roentgenogram of chest taken on October 12, 1944, showing a large metallic fragment in the left chest at the level of the 10th dorsal vertebra. The smaller fragment is outside the thoracic cavity in the tissues of the axilla.

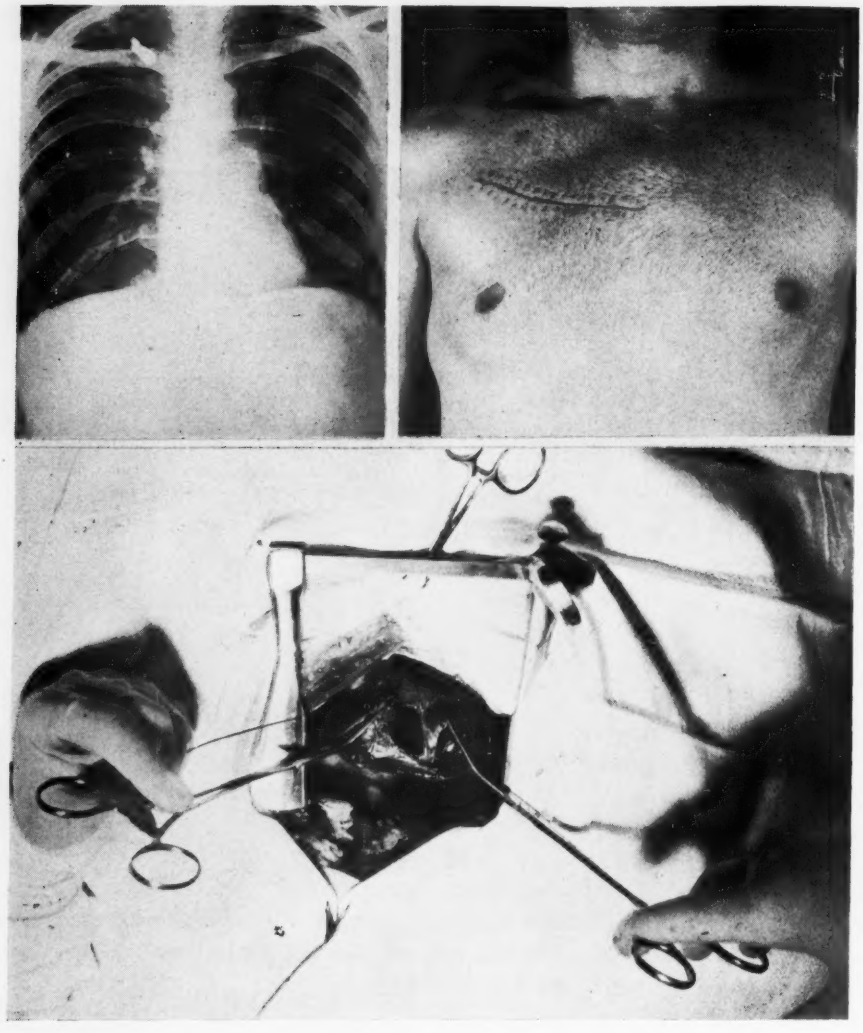
(B) Lateral view, also taken on October 12, 1944, showing the metallic fragment to be situated posteriorly.

COMMENT: This case is another illustration of a metallic foreign body being retained in the substance of the lung for many months without causing symptoms. The fact that this man did not develop a postoperative empyema may have been due to the penicillin (Fig. 6).

Case 7.—A soldier was wounded accidentally when a 60-mm. mortar shell fell short and exploded at 0930 hrs., May 2, 1944. He was struck by a shell fragment in the left lower chest and, on admission to a General Hospital, about two hours later, complained of severe, upper abdominal pain. Examination showed moderate shock, with rigidity and tenderness in the upper abdomen, and beginning dullness in both flanks. There was a wound approximately 15 cm. long in the midaxillary line, left, at the level of the tenth intercostal space, with a portion of the spleen herniating through the wound. Roentgenograms of the chest and abdomen were reported negative, both for pneumothorax and foreign bodies.

The patient was given plasma, and the abdomen was explored three hours and fifteen minutes after injury. The operative findings included a ruptured spleen, a 7-cm. rent in the left leaf of the diaphragm, two perforations of the stomach, a puncture wound on the inferior surface of the left lobe of the liver and blood and gastric contents in the peritoneal

6-A 6-C



6-B

FIG. 6.—Case 6: (A) Roentgenogram made May 23, 1945, showing the metallic shell fragment in the right upper lung field.

(B) Photograph made at operation on September 28, 1945. Traction on the wound edges has produced the appearance of a cavity which did not exist. The fragment can be seen in the depth of the space.

(C) Photograph of the patient made October 8, 1945, ten days after operation, showing the operative wound over the second right interspace.

cavity. The spleen was removed, and after suturing the perforations of the stomach and the rent in the diaphragm the wound was closed in layers without drainage. The puncture wound on the under surface of the liver was not explored. The wound of the chest wall was then débrided and closed. Subsequent to this the soldier developed a left empyema. He came under our care, September 19, 1944, with a discharging sinus at the site of a previous rib resection. The sinus was excised and a residual empyema cavity unroofed on September 25. Microscopic examination of the sinus tract showed "numerous tubercles with central necrosis and borders of granulomatous tissue." This procedure was also followed by a persistent sinus. On subsequent investigation this was found to connect with a bronchus and to extend through the substance of the lung to the diaphragm apparently along the course taken by the shell fragment. The soldier had to undergo two additional operative procedures before the tract was completely excised and permanent healing of the wound obtained. Examination of the tissue removed at these operations confirmed the diagnosis of tuberculosis.

COMMENT: This case is of particular interest because of the development of tuberculosis of the tissues at the site of injury. So far as is known this patient had never shown any previous manifestations of this disease. The complication supplies an adequate explanation for the chronicity of the process and the repeated failures to obtain satisfactory healing despite the establishment of adequate drainage. A satisfactory result was finally obtained only when all of the disease had been excised and the resulting defect closed by the approximation of well-nourished tissues.

Primary celiotomy was obviously the correct procedure and it seems wise that no effort was made to remove the shell fragment which was embedded in the liver. In consideration of the soldier's extensive injuries and condition at the time of operation, it also seems wise that the chest was not explored. Primary closure of the superficial layers of the wound of the chest wall after débridement, however, was contrary to the teachings of most military surgeons at the present time.

CONCLUSIONS

In conclusion, it would seem appropriate to direct attention briefly to the rapid advancement which has been made in the field of thoracic surgery since World War I. The dangers of open drainage in the early stages of empyema were appreciated before World War I was over, and the fall in mortality rate which followed has already been mentioned. After this, the means of controlling respiration by positive pressure were perfected and this made it possible to undertake with safety deliberate and meticulous operating inside the thoracic cavity. This soon led to a rapid advance in surgical technic and within a very short time operations like lobectomy and pneumonectomy (both of which had been tried before but abandoned because of high mortality) were being undertaken again and with a very reasonable mortality. In the past six or eight years the operative mortality for lobectomy has fallen to about two or three per cent and more recently esophagectomies, pericardiectomies, suture of heart wounds, ligation of patent ductus arteriosus and excision of intrathoracic neoplasms have become a daily occurrence. So there was good reason

to expect that the results of treatment of chest injuries in World War II would be superior to those of World War I. That this is true is apparent from the relatively low mortality rate for chest injuries and the low incidence of chronic empyema.

REFERENCES

1 Carter, B. N., and DeBakey, M. E.: Current Observations on War Wounds of the Chest. J. Thoracic Surg., **13**, 271, 1944.

2 Craham, E. A., and Bell, R. D.: Open Pneumothorax: Its Relation to the Treatment of Empyema. Am. J. Med. Sci., **156**, 839, 1918.

3 Graham, E. A.: Empyema Thoracis. St. Louis, C. V. Mosby Co., 1925.

4 Barrett, N. R., and Cleland, W. P.: Personal communication.

5 Cooper, F. W., Stead, A., Jr., and Warren, J. V.: The Beneficial Effect of Intravenous Infusions in Acute Pericardial Tamponade. ANNALS OF SURGERY, **120**, 822, 1944.

6 Davies, H. M., and Cooper, R.: War Injuries of the Chest. E. & S. Livingstone, Edinburgh, 1942, p. 57.

7 Edwards, A. T.: Cited from Bailey. (Bailey, H.: Surgery of Modern Warfare, Edinburgh, Ed. 2, I, 369, E. & S. Livingstone, 1942.)

NOTES ON OPERATIVE TECHNIC IN NEUROSURGERY

WILDER PENFIELD, M.D.

MONTREAL, CANADA

FROM THE DEPARTMENT OF NEUROLOGY AND NEUROSURGERY, MCGILL UNIVERSITY, AND THE MONTREAL NEUROLOGICAL INSTITUTE, MONTREAL, CANADA.

THE MINOR PRINCIPLES of operative technic to which a surgeon adheres are the product of his surgical inheritance, the traits of his character and his capacity for imitation. Neurosurgeons have borrowed freely from each other and I have learned much from my own colleagues, William Cone and Arthur Elvidge. Consequently, no claim is made to originality in this field. But it was Professor Allen Whipple who first called my attention to the importance of these minor principles of surgical technic. The following notes are, therefore, set down here by his grateful pupil and friend.

Classical Technic.—Harvey Cushing was the first superlative technician among neurosurgeons. Fastidious care in every detail of opening and closure of the skull was perhaps his greatest contribution to the operative technic of craniotomy. Fastidiousness was his by inheritance from Professor Halsted and as an inborn characteristic.

He made a habit of closing the dura after an osteoplastic craniotomy without drainage. On the other hand, he left the dura open under a subtemporal decompression and after a suboccipital craniotomy. He almost never drained a craniotomy wound. But he took great care to close the galea aponeurotica with a careful line of interrupted fine silk sutures. This was a technical maneuver of the greatest importance to which almost all neurosurgeons still adhere because it relieves the skin sutures of tension and prevents fistular drainage.

But Cushing found it necessary to puncture the scalp and aspirate fluid from beneath the aponeurosis frequently during the first ten postoperative days. That was his way of relieving tension on his unfastened bone flap and his undrained scalp, and it worked well in his hands, however tedious the dressings.

This set of technical procedures might be called the classical pattern. When one detail is altered many others must be changed. But to continue to adhere to it would be to miss the opportunity for advance.

Drainage.—A rubber drain through a small scalp incision, "stab wound," not far from the incision for an osteoplastic craniotomy, may serve to allow fluid to escape from outside the dura. If the inner end of the drain is placed inside the dura, fluid and air are allowed to escape from the intradural as well as the extradural space.

Such a drain should be covered with gauze and over that a layer of impermeable protective tissue, the borders of which are brought down to the sterile scalp surface on which sterile vaseline may be placed. This avoids any danger of retrograde contamination provided the drain is withdrawn within one to

three days. This type of drainage makes it possible to fasten the bone flap at one or two points with steel or tantalum wire if it seems desirable.

Cosmetic Note.—The bur holes of the bone may be covered with small round disks of sheet tantalum. This is preferable to replacement of bone buttons or bone fragments, for these implants shrink with the passage of years and most surgeons are distressed by the dimpled foreheads or, even worse, the dimpled bald heads that return to their consulting rooms from time to time.

Lumbar Puncture.—When bone flaps are fastened with wire they reunite with the surrounding bone of the skull much more rapidly and with less bone atrophy. But if the removal of tumor or scar has been so small as not to compensate for postoperative brain swelling then lumbar puncture, carried out more or less frequently, may become necessary in order to decrease intraventricular pressure temporarily. Punctures are rarely needed as long as drainage is used.

The old fear of lumbar puncture is no longer justified, provided a surgeon understands the syndromes of (1) midbrain compression due to temporal lobe herniation into the incisura tentorii (enlarging pupil and loss of reaction to light and failing consciousness, *etc.*); and (2) bulbar compression due to herniation of cerebellum into the foramen magnum (slowing pulse and slowing irregular breathing, *etc.*).

Aseptic Meningitis.—This is a term which may be applied to the meningismus and fever associated with the continuing escape of fluid from an operative field into the subarachnoid spaces at the base of the brain, the basal cisternae. Elevation of temperature, because of this, often continues for a week or two after operation. But it may persist for many weeks as a continuous state or as a recurring phenomenon separated by several days of freedom from symptoms. In the recurring type of aseptic meningitis there is sudden headache, fever, leukocytosis in the cerebrospinal fluid and nuchal rigidity.

The most frequent cause of persistent aseptic meningitis is an opening between one of the ventricles and the field of a large operative procedure. Through such an opening into the ventricle the fluid from about the operative blood clot passes through the ventricular system and into the basal cisterns. The second most frequent cause is a wide opening between cisterna magna and operative site.

To prevent this irritative state, care should be taken not to open through the ependymal wall of a ventricle. This is usually not difficult. If, however, a large opening is made into the ventricle the ependymal lining may be closed by a few loosely tied silk sutures. It is helpful to place fibrin film or a strip of gelatin sponge over the rent in the ependyma so as to be included within the sutures when they are tied.

In the posterior fossa, however, it may be impossible to prevent opening the arachnoid covering of the cisterna magna. But when the site of operation is the cerebellopontile angle care should be taken to make only a small decompressive opening in this arachnoidea which covers the cisterna magna.

Dural Defects.—When it seems advisable to close a dural defect after a

supratentorial craniotomy it is practically never necessary to resort to the use of a fascial transplant from an incision in another part of the body. Instead of this it is a simple procedure to split the outer layer from the inner layer of adjacent intact dura and to use the outer layer to fill in the defect. If this is not convenient or if the dura is very thin, the epicranium may be removed from adjacent skull and used as a transplant. These procedures provide a satisfactory dural substitute which is preferable to prepared membranes.

Decompression.—Subtemporal decompression by means of an opening in the dura over one temporal lobe, so that the brain may bulge outward against the elastic wall of the temporal muscle, still has a restricted field of usefulness, but it is an extremely small field. Decompression of the brain by means of removal of an expanding blood clot or tumor is a very much better procedure, for this removes the cause. In case it is not enough, internal decompression may be employed. By this term is meant the removal of relatively dispensable brain tissue.

For example, one frontal pole or the temporal lobe of the nondominant hemisphere may be removed, and even on the side of the dominant hemisphere the anterior end of the temporal lobe, *i.e.*, 4 to 5 cm. back from the tip of the lobe, may be removed without fear of aphasia.

Improvements and modifications of technic come each year. Men who are young in years, or in mind, are apt to accept them eagerly. Others are more cautious; but nothing can replace the rules of delicate handling of tissue introduced by Halsted.

New methods are not necessarily better methods, and the safest guide to progressive modification is an understanding of the basic principles of intracranial physiology and of wound healing.

REFERENCE

[1] Finlayson, Alister I., and Penfield, Wilder: Acute Postoperative Aseptic Leptomeningitis. Arch. Neurol. and Psychiat., **46**, 250, 1941.

POSTERIOR CORDOTOMY FOR RELIEF OF PHANTOM LIMB PAIN

J. Lawrence Pool, M.D.
New York, N. Y.

Phantom limb pain, as distinguished from phantom limb sensation or the pain due to sensitive neuromata of an amputated stump, is fortunately rare, for it constitutes a most difficult therapeutic problem. Various procedures such as revision of stump neuromata, neurectomy, rhizotomy, spinothalamic tractotomy,[3] and psychotherapy too often fail to afford relief. Extirpation of the appropriate sensory area from the cerebral cortex, while effective,[4] is open to the serious objection of potential postoperative epilepsy. Prefrontal lobotomy[18] is open to the same objection, plus the additional hazard of postoperative personality changes.

Another procedure has, therefore, been carried out, consisting of posterior cordotomy; that is, section of the posterior column and adjacent substantia gelatinosa of that part of the cord serving the amputated extremity. This procedure entails a minimal risk of postoperative complications, since none of the spinal cord is cut except the portion rendered unessential by virtue of the amputation.

By way of preface it should be stated that, in contradistinction to phantom limb *pain,* phantom limb "sensation" or "impression" is experienced by most amputees.[4, 6, 7, 8, 13] The absent member seems intact, numb, and fixed in one position as a rule. Despite initial posttraumatic discomfort in some cases, such patients usually become accustomed to this sensation, so that it does not constitute a therapeutic problem. Some amputees are also subject to acute lancinating or shocking pains whenever a sensitive neuroma is touched, jarred, or compressed.[8] This condition is not characteristic of true phantom limb pain, nor is the latter always reproduced by electrical stimulation of neuromata.[8] Relief of neuroma pain may be afforded by revision of the offending nerve end by resection, ligation,[7, 8] or injection with alcohol or formalin.[5] When the condition of the wound precludes local surgical intervention, it may then be necessary to resort to neurectomy at a point proximal to the stump, or to dorsal root section through an hemilaminectomy.

True phantom limb pain, occurring in approximately 6 per cent of all amputees,[7, 8] is severe, unremitting, and may be of two varieties, either of which may overshadow the other in severity—(1) burning pain; and (2) cramping pain.

The burning quality of phantom limb pain resembles that of causalgia[12, 16] and other conditions associated with neurovascular dysfunction.[20] For this reason, plus the fact that neurovascular pathology has an extremely high incidence in cases suffering phantom pain,[7] it may be postulated that the burning quality of phantom limb pain is primarily due to neurovascular and associated autonomic disturbances. This view is substantiated by the fact that sympathectomy has relieved phantom limb pain of this variety.

Certain patients, however, complain chiefly of the second, or cramped posture type of pain,[3, 4, 6, 13] which seems to clamp the limb in a tight, fixed position. Since this variety of pain seemed closely allied with disturbed proprioception, it was felt that proprioceptive impulses arising from foci of irritation in the spinal cord,[9] might be responsible for its perpetuation. This supposition is based on the fact that, in certain circumstances, nonpainful stimuli can produce painful reactions and sensations by the process of reënforcement[21] or facilitation.[14] The posterior column conveys the bulk of proprioceptive impulses from spinal cord to midbrain and thalamocortical levels.[15]

Posterior cordotomy was, therefore, carried out in the three patients reported below, with the original intention of sectioning only the posterior column related to the phantom limb. The planned procedure was modified, however, as described in the case reports.

CASE REPORTS

Case 1.—G. B., age 24, was wounded by multiple high explosive shell fragments in the left shoulder November 29, 1944. Amputation at the left shoulder was performed the same day. The patient then suffered marked discomfort continuously throughout the phantom limb, the discomfort being characterized by a sensation of persisting severe muscle cramp that was not only painful but seemed to maintain the limb in a fixed position, as if the forearm were flexed at 90 degrees and the fingers were held in a semi-clenched posture. An associated burning pain was slightly relieved by sympathetic block.

Operation.—December 12, 1945: Local anesthesia (1% procaine). Hemilaminectomy; posterior cordotomy (section of fasiculus cuneatus and substantia gelatinosa, left (at C5 and C6).

The left fasiculus cuneatus was transversely divided with a small scalpel blade to the depth of 3.5 mm. just below the 5th cervical laminal arch. On questioning the patient on the table, it was then found that the cramped sensation in the phantom hand was only partially relieved. Therefore, the same procedure was carried out 2.0 cm. distal to the first section, whereupon the patient stated that his original discomfort was almost completely relieved. It should be emphasized that the cord section was carried 2.5 mm. beyond the *lateral* margin of the posterior column, thus, passing through the substantia gelatinosa and part of the dorsal horn where local sensory nerve roots enter the cord and give rise to synaptic and collateral connections.

Following operation there was lasting though not complete relief of the cramping pain. The patient no longer looked anxious and apprehensive, but cheerful and relieved. Three months after operation he had gained 15 pounds, and was on his way to go home and to work.

COMMENT.—It is of interest that after the cordotomy he became aware of a persisting sense of numbness in the phantom hand, without apparent change in its position from the preoperative status. No postoperative sensory, motor, vasomotor, or reflex alterations could be elicited in the opposite upper extremity or in either lower extremity, nor was there a Horner's syndrome. However, from the level of the clavicle to the groin on the left (operated) side, it was noted that application of cool or warm objects to the skin produced an exaggerated and disagreeable sensation of cold and warmth, respectively, causing the patient to flinch. Pin-prick was not felt as acutely as in unaffected areas, and there was a constant sense of mild numbness and stiffness throughout this

area, although no impairment in perception of cutaneous figure-writing or vibratory or positional sensation could be found. These subjective and objective dysesthesias gradually disappeared during the course of the first eight weeks after operation.

Case 2.—M. S., age 31, was wounded by mortar shell fragments, May 25, 1945, so extensively that the entire left arm had to be amputated at the shoulder on the same day. The wound healed poorly and pus drained intermittently for several months. When examined, December 1, 1945, the stump was well healed, but the patient complained of a constant severe, tight cramp-like sensation in the phantom hand which seemed semiclenched. In addition, he had trigger areas in the stump which, when touched, accentuated his cramping pain and also produced a shooting, burning type of pain along the phantom arm. Revision of stump neuromata, sympathetic ganglion block, and, finally, section of the trunks of the affected brachial plexus were successfully performed, without significant benefit. A posterior cordotomy was, therefore, performed at the patient's request.

Operation.—December 12, 1945: Local anesthesia (1% procaine). The same procedure, at the same levels, was carried out as in Case 1. Almost complete relief was experienced immediately after the operation, but within 36 hours there was considerable return of the original pain, lasting improvement being estimated by the patient at approximately 20 per cent. The hand seemed to be in the same position as before operation; there was relief of the preoperative sensation of tightness, but not of the cramp.

Postoperatively, he noted a sense of stiffness over the entire left thoracic region from the clavicle to the 11th rib, with distortion of thermal and pain perception similar to that experienced by Case 1. There was no other postoperative neurologic change.

It is of interest (see discussion) that this patient had also been wounded in the region of the right or opposite brachial plexus, and sometimes suffered pain along the distribution of the right ulnar nerve. At such times, accentuation of the phantom limb pain occurred after as well as before cordotomy. He also observed that shaving the left side of his face induced a "pulling" sensation along the inner aspect of the left arm.

Three months postoperatively the phantom hand was still free of the preoperative sensation of tightness, though cramp-like pain persisted in the shoulder. The imagined posture of the phantom limb remained unaltered.

Since the burning pain continued, a high left dorsal sympathectomy was done (Smithwick procedure) on March 20, 1946. This afforded no additional relief, and it was, therefore, concluded that more drastic measures would probably be necessary, such as cortical extirpation.

Case 3.—L. K., age 25. In May, 1945, a very heavy timber dropped on the left arm, causing such a severe injury that the arm had to be amputated at the shoulder. Following amputation the patient experienced acute cramping and burning pains in the phantom hand, as well as acute hyperesthesia over the left pectoral region. Repeated sympathetic blocks failed to afford relief. It was felt, therefore, that section of the appropriate dorsal roots, rather than sympathectomy, offered the best chance of relief. On October 8, 1945, the spinal cord was exposed from C 5 to Th. 4, through an hemilaminectomy. The dorsal roots and portions of the ventral roots of C 6, 7, 8 could not be identified, having been avulsed at the time of the injury. Accordingly, it was possible to divide only the dorsal roots of C 5, Th. 1, 2, 3 and 4. Following this procedure there was almost complete relief of pectoral hyperesthesia, but only partial relief of phantom limb pain. At the insistence of the patient, therefore, a more radical procedure was undertaken.

Operation.—February 10, 1946: Endotracheal gas-oxygen-ether anesthesia. (1) Posterior cordotomy at C 5, left. (2) Sympathectomy, Th. 2-4, inclusive, left. The double procedure was carried out in the hope of dealing both with the cramp-like and also the burning type of pain.

Following operation this patient was comfortable for the first time since his injury. For approximately 14 days after cordotomy hypalgesia and thermal hyperesthesia were noted over the left thorax from the clavicular level to Th. 8. The phantom fingers seemed to be in the same posture one month after the combined operation, as before, but the hand now seemed to be attached to the shoulder instead of the wrist. The skin over and around the stump was dry; there was slight weakness of the peroneal muscles of the left leg and slight diminution of vibratory and position sense in the left foot, plus some reduction of pain and temperature perception over S 3-5 on the right. These signs were rapidly clearing up, and were attributed to edema of the left side of the spinal cord. In fact, this patient considered his last operation so successful that he recommended it to two fellow sufferers.

DISCUSSION.—Posterior cordotomy alone relieved one patient (Case 1) of cramping pain sufficiently to be considered therapeutically worth while. Another patient (Case 2) was only partially relieved by cordotomy, and subsequent sympathectomy afforded no further relief, so that neither procedure proved adequate in this instance. In the third patient (Case 3), whose relief proved most satisfactory, posterior cordotomy and sympathectomy were performed at the same time.

Since all these patients had been subjected to previous procedures (without benefit), the mere fact that surgery was undertaken can scarcely account for their improvement following posterior cordotomy. It is significant that spinothalamic tractotomy has not proved successful in this type of case.[3]

Transection of the dorsal column serving the amputated limb did not appreciably alter the imagined posture of the limb. This observation supports the view that imagined posture is a function of sensory complexes (probably thalamocortical) above the spinal level,[4, 6, 13] due to a "reverberating circuit."[11]

Alleviation of cramping pain by posterior cordotomy may be due, in part, to section of the posterior column, and, in part, to reduction of sensory impulses other than proprioceptive (a) by section of afferent fibers in the substantia gelatinosa; and (b) by interference with afferent collaterals running in, or close to, the substantia gelatinosa; that is, internuncial fibers[15] in the tract of Lissauer.

The fact that the cordotomy had to be extended into the substantia gelatinosa at two levels before significant relief was noted (Cases 1 and 2) substantiates the first view. The postoperative hypalgesia and thermal hyperesthesia, remote from the level of cordotomy in all three cases, supports the second view, for such an effect must have been due to section of ipsilateral, intersegmental sensory collaterals, since the spinothalamic tract serving the affected dermatomes lay in the opposite, untouched quadrant of the cord.

Since posterior cordotomy alone, or in conjunction with sympathectomy, diminishes phantom pain, it may be postulated that these procedures reduce the influx of abnormal impulses tending to maintain hyperactivity (by rein-

forcement) of suprasegmental circuits, such as the thalamocortical relays. Wolff comes to a similar conclusion in regard to other types of pain: "—— that reinforcement in certain instances does occur within the cortex is established."[21]

From the case studies presented above, it appears that the specific type of pain depends in some degree on the predominating type of abnormal "reinforcing" impulses. That is, impulses of predominantly proprioceptive character tend to perpetuate cramped-posture pain, while those of autonomic origin seem more closely related to the production of a burning type of pain. The severity of pain, on the other hand, to some extent seems related to the quantity of ascending impulses of various types, as judged by the fact that section of the substantia gelatinosa, and the various fibers therein, seemed to contribute to the relief of pain. In other words, dual factors, specific and quantitative, may be postulated as affecting the pain mechanisms just outlined. Studies of other pain mechanisms lend support to the dual concept.[1, 19]

Before closing the discussion mention should be made of the fact that in Case 2 sensory stimuli originating in dermatomes adjacent to the amputation site, induced dysesthesia in the phantom limb. Similar phenomena have been observed after other types of injury to the nervous system,[17] and are in keeping with laboratory experiments[10] showing that a sensory stimulus applied to the spinal cord is reflected at all levels in a degree that diminishes with distance.

The transitory postoperative hypalgesia in conjunction with hyperthermesthesia encountered in all the above patients is probably similar in nature to the paradoxical hyperalgesia in the presence of subnormal cutaneous sensation which occurs after certain incomplete peripheral nerve injuries or during recovery from nerve block. The same phenomenon has been described by Browder[2] following posterior cordotomy for relief of phantom limb pain in the lower extremity. This effect is probably due to physiologic disturbances of sensory relays within the affected segments of the spinal cord.

CONCLUSIONS

1. Relief of phantom limb pain may be achieved by posterior cordotomy alone, and by posterior cordotomy plus sympathectomy.

2. Phantom limb *pain* may be of two kinds, which may occur concurrently: (a) Burning pain, presumably of autonomic origin; and (b) cramped-posture pain, due in part to disturbance of proprioceptive circuits, which can be relieved by posterior cordotomy.

3. The imagined *posture* of a phantom limb appears to be due primarily to dysfunction of suprasegmental (thalamocortical) rather than segmental (spinal) circuits.

REFERENCES

[1] Bishop, G. H.: Responses to Electrical Stimulation of Single Sensory Units of Skin. J. Neurophysiol., **4**, Nos. 5–6, 361, Sept.-Nov., 1943.

[2] Browder, E. Jefferson: Personal communication, February 12, 1946.

[3] Coleman, C. C.: Surgical Treatment of the Nervous System: Bancroft, F. W., and Pilcher, C.. Philadelphia, J. B. Lippincott Co., 1946, p. 534.

[4] DeGutierrez-Mahoney, C. G.: The Treatment of Painful Phantom Limb by Removal of Post-Central Cortex. J. Neurosurg, **1**, No. 2, 156, March, 1944.

[5] Guttman, L., and Medawar, P. B.: The Chemical Inhibition of Fibre Regeneration and Neuroma Formation in Peripheral Nerves. J. Neurol. Psychiat., **5**, 130, 1942.

[6] Foerster, O.: Über das Phantom glied. Med. Klinik, **27**, 497, 1931.

[7] Hermann, L. G., and Gibbs, E. W.: Phantom Limb Pain: Its Relation to the Treatment of Large Nerves at the Time of Amputation. Am. J. Surg., **67**, 168, 1945.

[8] Livingston, K. E.: The Phantom Limb Syndrome: A Discussion of the Rôle of Major Peripheral Nerve Neuromas. J. Neurosurg., **2**, No. 3, 251, May, 1945.

[9] Livingston, W. R.: Pain Mechanisms: A Physiological Interpretation of Causalgia and its Related States. New York, Macmillan Co., 1943.

[10] Lloyd, D. P. C.: Mediation of Descending Long Spinal Reflex Activity. J. Neurophysiol., **5**, 435, 1942.

[11] Lorento, deNo. R.: Vestibulo-ocular Reflex Arc. Neurol. & Psychiat., **30**, 245, 1933.

[12] Mayfield, F. H., and Devine, J. W.: Causalgia. Surg., Gynec. & Obst., **80**, 631, 1945.

[13] Mitchell, S. W.: Injuries of Nerves and their Consequences. Philadelphia, J. B. Lippincott & Co., 1872, p. 377.

[14] Porter, E. L., and Taylor, A. W.: Facilitation of Flexion Reflex in Relation to Pain after Nerve Injuries (Causalgia). J. Neurophysiol., **8**, No. 5, 289, 1945.

[15] Mettler, F. W.: Neuroanatomy. 1942, The C. V. Mosby Company, St. Louis.

[16] Rasmussen, T. B., and Freedman, H.: Treatment of Causalgia: An Analysis of 100 Cases. J. Neurosurg., **3**, No. 2, 165, 1946.

[17] Travell, J., and Bigelow, N. H.: Referred Somatic Pain does not Follow a Simple Segmental Pattern. Federation Proc. Am. Soc. for Exp. Biol., **5**, 106, 1946.

[18] Walker, H. E.: Personal communication to Wolff, H. G.[21] Some Observations on Pain. Harvey Lecture, October 28, 1943.

[19] Walshe, F. M. R.: The Anatomy and Physiology of Cutaneous Sensibility: A Critical Review. Brain, **65**, 48, 1942.

[20] White, J. C., and Smithwick, R. H.: The Autonomic Nervous System: Anatomy, Physiology and Surgical Application. New York, Macmillan Co., 1941, 2nd Ed., p. 469.

[21] Wolff, H. G.: Some Observations on Pain. Harvey Lecture, October 28, 1943.

STREPTOMYCIN IN SURGICAL INFECTIONS
II. INFECTIONS OF THE GENITO-URINARY TRACT

CAPT. EDWIN J. PULASKI, M.C.,, A.U.S.

FROM THE HALLORAN GENERAL HOSPITAL, SECOND SERVICE COMMAND, STATEN ISLAND, NEW YORK.

A STUDY of the therapeutic value of streptomycin in surgical infections was begun in the Halloran General Hospital in July, 1945. The types of cases studied include battle wound infections, peritonitis, bacteriemias, infections of the respiratory tract, and infections of the genito-urinary tract. The laboratory aspects of this investigation have been reported in detail elsewhere.[1] This paper is a report on the experiences in the treatment of genito-urinary infections with streptomycin.

1. *Pharmacology:* Streptomycin hydrochloride (Merck) or the sulfate (Abbott, Pfizer, Squibb, and others) is dispensed as a fine yellow-orange crystalline powder, in ampoules containing 0.5 gram or one gram. It is standardized so that one gram contains 1,000,000 "S" units, each unit being equivalent to one microgram. Because of the size of unit, and of possible confusion with the unrelated penicillin unit, it is preferable to express streptomycin values in terms of weight. Hereafter, in this report, dosages will be given in terms of grams, and bacterial sensitivities and body fluid drug levels in terms of micrograms. For parenteral administration, the contents of an ampoule are dissolved by adding sufficient sterile isotonic saline to make a ten per cent solution, for example, ten cc. to the one-gram ampoule.

It has been amply demonstrated[2] that streptomycin reaches the blood stream shortly after intramuscular administration, and that it is excreted rapidly by the kidneys. The rate of excretion is slower than that of penicillin, allowing the drug to be given at less frequent intervals. The intramuscular method of administration is preferred to intravenous injection, which has no advantage, and which is attended by the danger of occasional acute toxic reactions. If the drug is given orally, very little of the streptomycin diffuses into the blood stream, and little or none of it appears in the urine. For this reason, oral administration is worthless in genito-urinary infections, and is limited to those diseases in which a high intra-enteric concentration is desirable.

2. *Dosage:* The first group of patients selected for streptomycin therapy in this hospital were those with spinal cord injuries. These patients are notoriously subject to various urinary tract infections and their sequelae, and they have been treated heretofore with penicillin, sulfonamides and other urinary tract antiseptics with variable success. Seven patients with polybacterial infections were treated with 0.2 gram (200,000 "S" units) of streptomycin intramuscularly every four hours, for a total of 18 doses, or 3.6 grams each. In two cases the results were considered good, while in the five others, the organisms reappeared and the pyuria recurred after a temporary slight improvement. To five other patients 0.15 grams was then given every three hours for 24 doses, for the same total dosage of 3.6 grams each. The results

were the same as in the first group of patients. The organisms became streptomycin-resistant. By this time it became apparent that larger doses of streptomycin would be required, and that even then, the outcome of treatment would be dependent to some degree on complicating factors present in addition to the infections. Another group of four patients each received 0.375 grams of streptomycin, administered every three hours for 24 doses, or a total of nine grams. The results were better. In each instance the urine cleared in the second day of treatment, and remained so. The *nonhemolytic Streptococcus* was found on culture of some of the urines after treatment, but its presence was not associated with clinical evidence of infection. All other organisms disappeared. A more detailed report of these earlier experiences with streptomycin treatment of urinary tract infections in patients with spinal cord injuries will be published by Kleinman and Shearer.[3]

With data from these cases as a background, the author undertook detailed study of a series of patients with genito-urinary tract infections, to determine the exact limitations and indications for streptomycin. On the basis of experience obtained with a large series of battle wound infections, the dosage scheme of 0.4 grams of streptomycin dissolved in four cc. sterile isotonic saline, administered intramuscularly every four hours, was adopted. It was found advisable to mix one cc. of one per cent procaine with the four cc. of streptomycin solution, to alleviate the pain which occurs following injection. Typical streptomycin assays of blood serum and urine with this dosage are listed in Table I. The levels shown in the table are sufficient to sterilize the

TABLE I

CONCENTRATIONS OF STREPTOMYCIN IN BLOOD AND URINE

Case No.	Blood Serum Assay	Urine Assay
22*	8–16 U./cc.	73– 153 U./cc.
27	4–16	2000 +
28*	16–32	64– 256
29*	32–32	128– 256
40	4–32	2000–2000 +
41	4–32	1000–4000
42	8–16	500–2000
45	8–32	500–4000
53	8	500–2000
54	8–16	500–2000 +
59	4–16	500–2000
66	8–16	512–1000
69	8– 8	128–1024
70	4–16	128–1024
72	4– 8	128–1024
74	4–16	1024–2048
76	4–16	1024–4096

* Marked impairment of renal function.

urines, provided the bacteria are not naturally resistant, that resistance has not been produced by previous underdosage, that renal function is adequate, and that there are no unsterilizable foci, caused by calculi or undrained abscesses. Streptomycin in concentrations above 1000 U./cc. reduces alkaline copper (Benedict's reagent) solutions. This reaction can be used as a rough

guide to determine the urine streptomycin level when facilities are not available for the more complicated exact assay of the drug.

3. *Bacteriology:* Routinely, urine specimens are cultured prior to treatment, and are repeated daily during therapy, then once weekly thereafter for two or more weeks. In males, specimens are obtained by voiding into sterile containers, but in indicated cases, urethral or ureteral catheterization is performed. All specimens are cultured aerobically and anaerobically. Each bacterial species is isolated in pure culture and tested for streptomycin sensitivity.

TABLE II

SUSCEPTIBILITY TO STREPTOMYCIN OF BACTERIA FROM 63 URINARY TRACT INFECTIONS

	Total No. of Strains	Number of Strains Inhibited by Streptomycin								
	Micrograms per cc.	0.5 U./cc.	1.0 U.	2.0 U.	4.0 U.	8 U.	16 U.	32 U.	64 U.	128 U.
Strep., nonhem.	46	7		2	12	6	14	4		1*
P. vulgaris	40			5	8	7	15	2	3	
A. aerogenes	29		2	5	6	5	4	2	3	2*
E. coli	22		1	5	3	8	3	2		
Staph. aureus	22	10	3		3	1				5*
K. pneumoniae	14		1	4	1	3	3		1	1*
Ps. aeruginosa	14					3	7	1		3*
Strep., hem.	7				3	3				1*
Strep. viridans	7				1	1	2			3*
Totals	201	17	7	21	37	37	48	11	7	16*

* Streptomycin-resistant.

Table II summarizes the 201 aerobic bacterial flora grown from the urines of 63 patients, and their sensitivity in broth to streptomycin. It is evident from this table, that most of the infections encountered are polybacterial in character. *Streptococcus nonhemolyticus (fecalis)* and the gram-negative bacteria are the predominating etiologic organisms in genito-urinary infections. The great majority of bacteria listed are sensitive *in vitro* to 16 (or less) U. per cc. Sixteen strains of a total of 201 (eight per cent) were found to be naturally resistant, and ten of these are gram-positive cocci. The susceptibility to streptomycin of the gram-negative bacilli and of the *nonhemolytic Streptococci* is of utmost clinical importance, in view of the fact that these organisms usually are indifferent to the action of penicillin and the sulfonamides.

4. *Clinical Investigation:* A special ward, adjacent to the Urologic Ward, has been set up, where complete and independent control of patients receiving streptomycin is effected. In addition to routine work-up before starting treatment, the following laboratory studies are made: complete blood count, sedimentation rate, hematocrit, blood urea nitrogen, urinalysis, and the already mentioned identification of the etiologic organisms and determination of their susceptibility to streptomycin. Urinalyses are repeated daily during treatment and once or twice weekly thereafter for two weeks. Intake and output measurements of fluid are maintained during the period of drug administration.

Streptomycin blood serum levels are made daily on blood which is drawn just prior to a scheduled injection, while urine assays are determined on 24-hour collections of urine. In addition, any other preliminary studies are accomplished which will give information on the results of therapy on the infection. Blood pressures are taken every two hours for 12 hours with every new batch of drug. Concomitant malnutrition, anemia, general debility and other factors are evaluated and treated as encountered (all data derived from study of these cases are assembled on standard streptomycin form sheets).

TABLE III

INFECTION IN THE URINARY TRACT IN PATIENTS WITH SPINAL CORD INJURIES

Dosage Scheme: 0.4 Gram Intramuscularly Every 4 Hours

Case No.	Diagnosis	Bacteriology and Strep.-sens.	Days Treated	Result
1	Recurrent pyelocystitis with acute episode	*A. aerog.*, 2 U. *E. coli*, 4 U. *Hem. Strep.*, 8 U.	3	Good. Urine sterilized, temperature subsided
22	Pyelocystitis, pyonephrosis with renal calculi, left, uremia	*A. aerog.*, 2 U. *E. coli*, 8 U. *B. proteus*, 8 U. *Nonhem. Strep.*, 8 U.	5	Failure. Poor renal function resulted in low urine drug concentration. Calculi are nonsterilizable. Bacteria became drug-fast
40	Severe chronic cystitis, persistent suprapubic fistula with suppuration	*A. aerog.*, >128 U. *K. pneu.*, >128 U. *Staph. aureus*, 8 U. *Anaerobic cocci*	6	Failure. Temporary reduction in bacterial colony count and pus cells in urine, followed by prompt recurrence of severe pyuria
42	Recurrent pyelocystitis with persistent suprapubic fistula	*A. aerog.*, > 128 U. *Nonhem. Strep.*, >128 U. *Viridans Strep.*, >128 U.	5	Failure. Organisms insensitive. No improvement resulted from subsequent continuous infusion of streptomycin into the bladder *via* Foley catheter
59	Chronic pyelocystitis	*A. aerog.*, 2 U. Anaerobic coccus Anaerobic Strep.	3	Good. Cultures negative after 3 days treatment. No recurrence
76	Chronic cystitis	*Staph. aureus*, 64 U. *Viridans Strep.*, 32 U.	6.5	Good. Urine cleared though *Staph. aureus* persisted. Combined penicillin and streptomycin sterilized the urine
24	Recurrent pyelonephritis, bladder calculi, and right vesico-ureteral reflux. (Had previous streptomycin therapy.)	*Ps. aerog.*, 128 U. *B. proteus*, >128 U. *Nonhem. Strep.*, >128 U. *Staph. aureus*, 0.5 U.	3	Failure. Previous drug administration made organisms insusceptible
69	Recurrent pyelonephritis, chronic urethritis and prostatitis. (Had previous streptomycin therapy.)	*Staph. aureus*, >128 U. *Hem. Strep.*, 64 U. *B. proteus*, >128 U.	3	Doubtful. *Hem. strep.* disappeared. Urethral discharge ceased, bladder capacity increased, automaticity improved

5. *Evaluation of Results:* (a) Table III summarizes the outcome of urinary tract infections in eight paraplegics treated with streptomycin. All of these patients had varying degrees of neurogenic bladders, and have had suprapubic cystostomies performed overseas, arriving at this hospital with severe urinary tract infections. All had received penicillin and sulfonamides without result. In three instances the streptomycin effected a prompt, dramatic and lasting sterilization of the urine. Each of these three had no suprapubic fistula, no residual urine, and excellent renal function. The organisms

were highly susceptible to streptomycin in each case. Among the five failures, one patient (Case 22) had uremia due to obstruction of one kidney by calculi and of the other by pyonephrosis. In retrospect, it would have been advisable to have waited for improvement in renal function, which followed bilateral ureteral catheter drainage. The other four failures, on reconsideration, should not have been given streptomycin. Two cases (Cases 40 and 42) had naturally resistant organisms, and, therefore, therapy was futile. They emphasize the importance of delaying treatment until bacterial sensitivities are known. The last two failures in this series were in-patients who had previous streptomycin therapy, and emphasizes the importance of the fact that underdosage rapidly produces permanent drug resistance, since resistant bacteria propagate resistant bacteria.

(b) Table IV shows the results of treatment of 13 patients with non-venereal genito-urinary tract infections. In seven patients with cystitis and pyelonephritis, the urine cleared within 24 to 48 hours, and remained sterile thereafter. One of these patients (Case 41) had an associated epididymitis which subsided rapidly. In another (Case 34) streptomycin was continued for nine days while treating an associated chronic osteomyelitis of the ilium, which improved in conjunction with sequestrectomy. The remaining five of the seven patients received only three days of treatment (7.2 grams or 7,200,000 units). Of the six failures, Case 28 improved clinically, but the *Ps. aeruginosa,* originally sensitive to four U./cc., became resistant to over 2,000 U./cc. This patient had an atonic ureter, a dilated pelvis with retention, and an indwelling pyelostomy tube, and illustrates the importance of obtaining good drainage and removing tubes. Case 29 (Chart 1) was treated for seven days, during which he was critically ill with a bacteriemia, secondary to a right pyonephrosis for which indwelling ureteral catheter drainage was instituted. Renal function was poor bilaterally, and resulted in very high blood levels of the drug and very low urine levels. The bacteriemia subsided, repeated blood cultures becoming negative, but his urinary tract infection did not clear-up. The offending organism, *A. aerogenes,* originally susceptible to 4 U./cc. streptomycin, became resistant to over 2,000 U./cc. Cases 53 and 66 are considered failures, even though the patients remain improved clinically. The gram-negative bacteria disappeared during treatment but the gram-positive cocci, naturally resistant in these two cases, remained after treatment. Both of these cases had small, silent calculi in the calices, for which surgery was not indicated at the time. It remains to be proved whether complete sterilization of the urine can be achieved in the presence of calculi when the infection is due to susceptible bacteria. Case 45 was a severe chronic prostatitis with a chronic gleet, whose prostatic secretion was almost pure pus. Although the urethral discharge stopped and the urine cleared, the prostatic fluid remained purulent. It is of interest that no streptomycin could be assayed in the prostatic fluid. It is possible that more beneficial results might be forthcoming, in such a case, if better prostatic drainage is established during systemic streptomycin therapy by repeated prostatic massage. Case 70 continues to show the resis-

tant *Strep. viridans* in the urine, but is clinically improved. This patient had a chronic interstitial cystitis and a contracted bladder. The bladder capacity was 30 cc. before treatment, and he had to urinate every 10 to 15 minutes. Following treatment the capacity of the bladder went up to 90 cc. with diminution of frequency and spasm. He is showing progressive improvement without further chemotherapy.

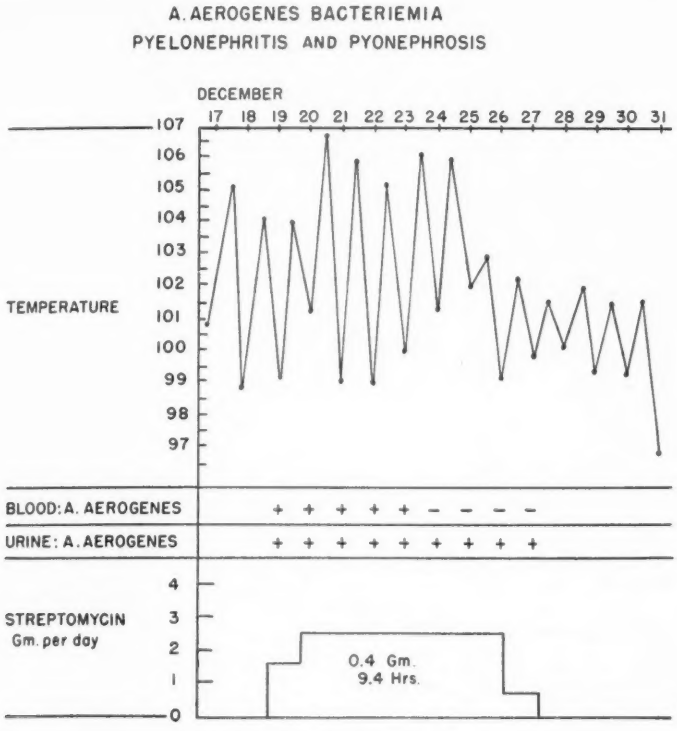


CHART I.

(c) In Table V are presented two cases in which streptomycin was instilled into the urinary tract directly. Both are considered failures from the bacteriologic standpoint, although there was clinical improvement. Case 14, an infected hydroureter due to stricture, received intra-ureteral instillations of 150,000 U. of streptomycin in 15 cc. of isotonic saline (10,000 U./cc.) every two hours for 48 hours. The gross pyuria subsided and the urine remains clear, but the cultures remain positive for *B. proteus*. Case 19, in whom a stag-horn calculus dropped from the kidney pelvis and caused obstruction at the middle third of the ureter, was operated upon, but, following extraction of the calculus from the ureter, there was a gush of thick pus. A catheter was inserted up to the kidney pelvis through the ureterotomy. Postoperatively, 10 cc. of streptomycin solution, 5,000 U./cc., was instilled, through the catheter twice daily, for 20 days. The urinary drainage became clear, but did not be-

come sterile. The wound healed rapidly following removal of the catheter. The patient had one large calculus in the bladder (3 cm. in diameter) and several smaller calculi. Since removal of these by litholapaxy, the patient's urinary tract infection has subsided.

TABLE IV

INFECTIONS IN THE URINARY TRACT: 13 CASES

Dosage Scheme. 0.4 Gram Streptomycin Intramuscularly Every 4 Hours

Case No.	Diagnosis	Bacteriology and Strep.-sens.	Days Treated	Result
10	Recurrent cystitis, posterior urethritis	*E. coli*, 4 U.	3	Good. Urine cleared in first 24 hours of treatment—has remained so
27	Chronic pyelonephritis associated with recurrent calculi requiring ureterolithotomy	*E. coli*, 2 U. *Staph. aureus*, 0.5 U. *Nonhem. Strep.*, —		Good. Urine became sterile. No recurrence
28	Hydropyonephrosis. Postpyeloplasty, ureterolysis and pyelostomy	*Ps. aerug.*, 4 U. *Viridans Strep.*, 16 U. *Staph. aureus*, 0.5 U.	3	Doubtful. Temperature subsided with change from Penicillin to streptomycin but *Ps. aeruginosa* persisted, became drug fast
29	Pyelonephritis, pyonephrosis, bacteriemia	*A. aerog.*, 4 U.	7	Doubtful. Blood stream cleared but urine did not. Poor renal function, low drug levels in urine, high levels in blood. Organisms in urine became resistant
34	Cystitis, fractured pelvis, with osteomyelitis	*E. coli*, 8 U. *B. proteus*, 8 U. *Strep. viridans*, 8 U.	9	Good. Cystitis cleared in 2 days of treatment. Additional therapy was for osteomyelitis
41	Cystitis and epididymitis	*K. pneu.*, 2 U. *Staph. aureus*, 4 U. Diphtheroid bacilli, 2 U.	4.5	Good. Urine cleared after 24 hours, inflammatory reaction in the epididymis resolved. No recurrence
54	Chronic pyelonephritis	*A. aerog.*, 4 U. *Anaerobic nonhem. Strep.*, —	3.5	Good. Urine cleared in 24 hours and has remained so
72	Chronic cystitis	*A. aerog.*, 4 U. *E. coli*, 8 U. *Staph. aureus*, 0.5 U.	3	Good. Urine sterilized and has remained crystal clear
74	Chronic pyelonephritis	*B. proteus*, 2 U. *Staph. aureus*, 1 U. *Nonhem. Strep.*, 2 U.	3	Good. Prompt response with sterilization of urine without recurrence
53	Chronic pyelonephritis with small silent renal calculi	*B. proteus*, 8 U. *P. morganii*, 8 U. *Ps. aerug.*, 8 U. *Hem. Staph. aureus*, >128 U.	5	Fair. Urine cleared. Pus cells became rare, but *Staph. aureus* remains
66	Pyelonephritis with small silent left renal calculi	*A. aerog.*, 8 U. *E. coli*, 16 U. *Hem. Staph. aureus*, 128 U. *Hem. Strep.—beta*, 128 U.	6	Doubtful. Resistant gram-positive cocci disappeared after combined streptomycin and penicillin only to reappear after cessation of treatment
45	Chronic prostatitis and cystitis	*A. aerog.*, 4 U. Micrococci, 0.5 U. Diphtheroid bacilli, 0.5 U.	6	Doubtful. Morning drop ceased and urine cleared partially. The foci in the prostate remained. No measurable streptomycin level in prostatic fluid
70	Chronic interstitial cystitis and prostatitis, contracted bladder	*Staph. aureus*, 4 U. *Viridans Strep.*, >128 U.	5	Failure. *Strep. viridans* unaffected

DISCUSSION AND SUMMARY

During the past nine months the use of streptomycin in a variety of urinary tract infections has revealed indications and contraindications for the use of this antibiotic. The exact limits for usage of this drug is still under investigation. The drug shows its most important action against the gram-negative organisms including *E. coli, P. vulgaris, A. aerogenes, K. pneumoniae, Ps. aeruginosa,* and others. Not all of the species in each of these groups are susceptible to streptomycin. Of additional significance is the potency of the drug against the gram-positive cocci, particularly the *nonhemolytic Streptococcus.* It has been possible to sterilize infections of all portions of the genito-urinary tract, except the prostate, due to these organisms.

TABLE V

GENITO-URINARY INFECTIONS TREATED WITH LOCAL STREPTOMYCIN

Case No.	Diagnosis	Bacteriology and Streptomycin Sensitivity	Scheme of Treatment	Condition at End of Streptomycin Course	Final Result
14	Congenital hydroureter, infected, with stricture at ureterovesical junction	*B. proteus,* 8 U. *Hem. Staph. aureus,* 128 U., *Hem. Strep.,* 8 U.	15 cc., Strep. sol., 10,000 U./cc. injected into ureteral catheters q.2.h. for 48 hrs. (1.7 Gm.)	Urine changed from cloudy to crystal clear but bacteria persisted as before treatment, became resistant	Urine continues to harbor *B. proteus,* but the specimens remain clear
19	Stag-horn calculus in midureter, rt., removed. Wound infection	*Hem. Strep.,*— *B. proteus,* 4 U. *A. aerog.,* 64 U.	10 cc., 5,000 U./cc. sol. instilled into wound twice daily for 10 days (1.0 Gm.)	The wound infection subsided, wound closed, urine became clear but not bacteria free	Persistence of bladder infection due to calculi in bladder. Infection cleared after litholapaxy

It has been shown that streptomycin action is greater in alkaline media[4] and alkalinization of the urine has been performed in several cases, prior to institution of streptomycin therapy. However, in case urea-splitting organisms, *(B. proteus)* are present, the advantages of alkalinizing the urine are offset by the increased rapidity of bacterial growth, plus the fact that in alkaline media there is greater tendency to precipitation of calcium phosphate. This combination of complicating factors is of importance in our paraplegias and orthopedic cases where the tendency to form calculi of recumbency is so great. This tendency toward calculus formation is also of importance and must be watched when we restrict the fluid intake in order to increase the urinary streptomycin level. Our data indicates that urinary streptomycin levels from 500 micrograms (U.) per cc. to 2,000 micrograms (U.) per cc. can be achieved by restricting the fluid intake to 2,500 cc. per day and administering streptomycin in doses of 0.4 gram intramuscularly every four hours. These levels are sufficient to sterilize most urines when the bacteria are susceptible and when there are no complicating factors.

Preferably, paraplegics should be treated only after they have automatic bladders and closed cystostomy wounds. The skin of these patients is notorious for harboring fecal organisms which are not eradicated by routine

hygienic measures. If catheterizations are needed during or following treatment, drug-resistant reinfection may result. In this group of patients, with spinal cord injuries, where such contraindications are present, streptomycin therapy should be reserved only for those who have uncontrolled, severe, upper tract infections or actual septicemia.

In view of the fact that only sensitive species of organisms in the group of gram-negative bacteria and gram-positive cocci respond to streptomycin, provided dosage is adequate, and because irreversible resistance of bacteria follows inadequate doses of drug, the cases selected for treatment must be rigidly controlled, lest the future value of streptomycin be destroyed for that particular patient.

The drug should not be used in instances of infection associated with uncompleted surgery, such as the presence of operable calculi. However, the drug may be given immediately before operation and during the patient's postoperative course. The drug should not be given where repeated catheterization or instrumentation which may reintroduce infection is required. Where there is a residual urine or where the patient has indwelling urethral catheters or pyelostomy or nephrostomy tubes, streptomycin should be delayed until these drainage tubes are removed. The drug is ineffective in instances of suppuration where surgical drainage has not been instituted.

In the present of small calculi in the calices for which surgical treatment is not indicated, further investigation is necessary to determine if a sterile urine can be achieved following the use of intensive treatment.

For local treatment, streptomycin has been used in saline solutions. Local application has the advantage of securing immediate high concentrations within the area of instillation, and, at the same time, permits considerable economy in the use of the drug. Irrigation of the kidney pelvis has been performed with solutions of streptomycin containing 5,000 and 10,000 micrograms (U.) per cubic centimeter. However, the mode of treatment must be individualized for each case. There is no convincing evidence to date of any advantage in urinary tract infections of local treatment alone over systemic streptomycin therapy.

The effectiveness of the drug in genito-urinary tuberculosis has not been evaluated. Being an hemotogenous infection, widespread throughout the body and manifested by an open lesion in one or both kidneys, systemic therapy and tremendous doses over a long period of time will be necessary and these cases will require considerable study. For the present, it is felt that the treatment of unilateral ulcerocavernous type of renal tuberculosis is still surgical. The effectiveness of local application of the drug for postnephrectomy tuberculous sinus tracts also requires further study.

In instances where a mixed urinary tract infection of gram-positive and gram-negative organisms exists, combined therapy using both streptomycin and penicillin has been found to be of value. There is no contraindication to combining the two antibiotics.

It is emphasized that in the usual case of infection in the genito-urinary

tract, three days of systemic streptomycin therapy, with the dosage recommended, is adequate. No advantage has been demonstrated with more prolonged treatment. It has not been found necessary to keep patients in bed during administration of streptomycin, if the patient's condition permits him to be up and about. There have been no serious drug reactions with these short courses of therapy. Pain at the sites of injection is usual. It is advisable to rotate the injections between the deltoids and gluteal muscles. Fall in blood pressure, asymtomatic except for mild headache and dizziness, has been noted following administration of some batches of the drug. In one case a diffuse morbilliform rash occurred which disappeared on withdrawal of the drug. Traces of "sugar" in the urine may be reported while the patient is undergoing streptomycin therapy. It is reiterated that this phenomenon is due, in part, to the reducing action of high concentrations of streptomycin on alkaline copper solutions. Blood sugar determinations on these patients are normal.

CONCLUSIONS

1. Forty cases of urinary tract infections treated with streptomycin at the Halloran General Hospital indicate that this antibiotic is a potent addition to the armamentarium of the urologist, particularly against the gram-negative bacteria, and the gram-positive cocci.

2. Cases selected for this treatment should be rigidly controlled for bacterial susceptibility, adequate renal function, and absence of urinary tract obstruction or calculi. Successful therapy depends on a free flow of urine, susceptible bacteria and adequate dosage.

Acknowledgment: The author received valuable advice and assistance in the management of the cases presented from Col. T. P. Shearer and Capt. J. H. Winer, of the Urological Service. The laboratory work was ably performed by Misses E. H. Thomas and J. E. Limb.

REFERENCES

[1] Pulaski, E. J., and Sprinz, H.: Streptomycin in Surgical Infections. I. Laboratory Studies. In press.

[2] Zintel, H. A., Flippin, H. F., Nichols, A. C., Wiley, M. M., and Rhoads, J. E.: Studies on Streptomycin in Man: I. Absorption, Distribution, Excretion and Toxicity. Am. J. Med. Sci., **210**, 421–431, October, 1945.
Anderson, D. G., and Jewell, M.: The Absorption, Excretion and Toxicity of Streptomycin in Man. New Eng. J. Med., **233**, 485–491, October 25, 1945.
Heilman, D. H., Heilman, F. R., Hinshaw, H. C., Nichols, D. R., and Herrell, W. E.: Streptomycin: Absorption, Diffusion, Excretion and Toxicity. Am. J. Med. Sci., **210**, 576–584, November, 1945.

[3] Kleinman, A. M., and Shearer, T. P.: Streptomycin Therapy of Urinary Tract Infections. In press.

[4] Foster, J. W., and Woodruff, H. B.: Microbiological Aspects of Streptothricin: II. Antibiotic Activity of Streptothricin. Arch, Biochem., **3**, 241–255, December, 1943.

[5] Herrell, W. E., and Nichols, D. R.: The Clinical Use of Streptomycin: A Study of Forty-five Cases. Proc. Staff Meet., Mayo Clin., **20**, 449–462, November 28, 1945.

ANTRAL GASTRITIS AND SPASM: THEIR CLINICAL AND SURGICAL SIGNIFICANCE

JAMES W. R. RENNIE, F.R.C.S. (ED.)
WINNIPEG, MAN.

DURING THE PAST TEN YEARS on the North American continent with the use of the "spot-film device" for the study of the mucosal patterns of the stomach by radiography, and with the extended use of the flexible gastroscope, due to the efforts of Schindler, the diagnosis of gastritis has become a problem to the radiologist and the surgeon especially in those cases where there is ulceration or hypertrophic processes which may simulate neoplasm of the stomach. Apart from a type of hypertrophic gastritis which produces giant rugae on the greater curvature of the stomach, and which may be mistaken for a neoplastic defect,[3, 7] the most difficulty to the surgeon from a clinical and surgical point of view is caused by the variety labelled "antral gastritis"[5] or "hypertrophic antrum gastritis."[1] Although spasm or inflammation may involve any part of the stomach, they are more commonly observed in the antrum. As this part of the stomach is a common site of carcinoma, antral gastritis and spasm are of particular importance to the surgeon because of the difficulties that arise in differential diagnosis. The internist on the other hand is mainly interested in those cases which fit mainly into the classification of gastritis developed by Schindler who differentiates: (1) Superficial gastritis; (2) atrophic gastritis; (3) hypertrophic gastritis; and (4) gastritis of the postoperative stomach. This classification does not greatly assist the radiologist who is able usually to distinguish only the hypertrophic type, and referring as it does to the mucosal lesions as seen by the gastroscopist it does not distinguish the variety of inflammatory lesions that are seen in the antrum. There is also serious doubt that the first type, superficial gastritis, is always clearly distinguishable, as the reddening and congestion described in this type are known to occur normally during periods of emotion such as anger. Nevertheless, it is generally agreed that the gastroscopist, particularly in the body of the stomach, can more easily and with more certainty make a diagnosis of gastritis than the radiologist.

Because it is the radiologist who, after perhaps a test meal, makes the initial examination of the stomach of a patient with gastric complaints, a great deal of responsibility devolves on him to correctly assess the amount of spasm in the antrum or any disturbance of antral systole[5] which he may see during the fluoroscopic examination, because it is his judgment of this spasm which determines largely the diagnosis of antral spasm. If the spasm is marked or persistent then the radiographs may show this persistent spasm in serial films as an elongation and narrowing of the antrum, giving a picture that is very similar to that of some cases of antral gastritis. Also during fluoroscopic examination, and assisted by radiographic studies of the mucosal pattern of the antrum, he must estimate any rigidity or abnormality of the normal mucosal folds before

making a diagnosis of antral gastritis. In our experience, a diagnosis of localized prepyloric hypertrophic gastritis has been made too frequently by radiologists in patients showing some degree of antral spasm with radiographic evidence of marked folds when on gastroscopic examination no evidence of any inflammatory process could be seen, and even the folds were obliterated by the distention necessary to the examination. This difficulty was foreseen by Gorsell,[4] in 1923, when he stated that: "Great experience and thorough comparative investigation are necessary before we are able to distinguish the pathologic types of the relief from the normal ones, and to separate the outlines formed by the defects or infiltrations of the intestinal wall from the relief of a contracted mucous membrane." And, more particularly, the fervent hope of

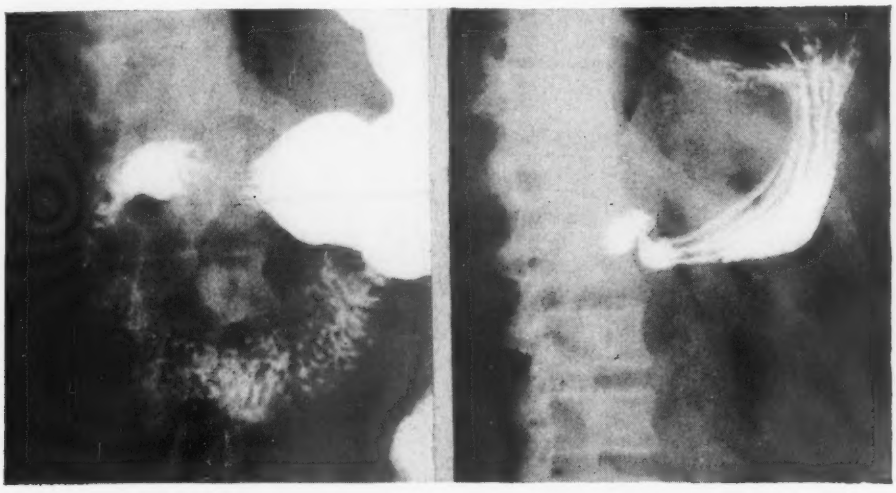


FIG. 1 FIG. 2

FIG. 1.—Case 1: Antral spasm, slight indentation of duodenal cap. Normal folds.
FIG. 2.—Case 1: Normal stomach one year later. Border folds of Chaoul clearly seen.

Kirklin,[8] in 1937, "further I hope that neither the roentgenologic and the gastroscopic diagnosis of gastritis will become common until the morbid anatomy of the disease, its right to be considered a pathologic entity and its clinical significance become better understood and more firmly established," still holds a great deal of truth today. Therefore, it is desirable that the diagnosis of antral gastritis be made only in those cases where there is demonstrable stiffening and irregularity of the antral mucosal folds or presence of an inflammatory filling defect, or where definite signs of inflammation are seen on gastroscopic examination. The degree of corelation between the roentgenologic and gastroscopic diagnosis of gastritis is stated by Renshaw[13] to be 93 per cent. In 842 cases, a positive diagnosis of gastritis was made in 17.7 per cent where there was a negative roentgenologic examination, and in 7.9 per cent of cases disease was excluded where a positive diagnosis of gastritis had been made by the radiologist.

The symptomatology of antral spasm and gastritis, unfortunately, presents no classical pattern such as is usually stated for peptic ulcer, carcinoma of the stomach or gallbladder disease, but is a peculiar combination of the symptoms of all three conditions. Pain in the epigastrium is the outstanding symptom. The pain bears no constant relation to food, being sometimes relieved, but more often made worse by eating. Anorexia with weight loss is common, and distaste for fats and heavy fried foods is common. In antral gastritis, hemorrhage is said to occur in 19.7 per cent of cases (Benedict).[2] In reviewing 34 cases of antral spasm found during 487 consecutive roentgenologic examinations of the stomach, it was found that these cases had an amazing similarity in their

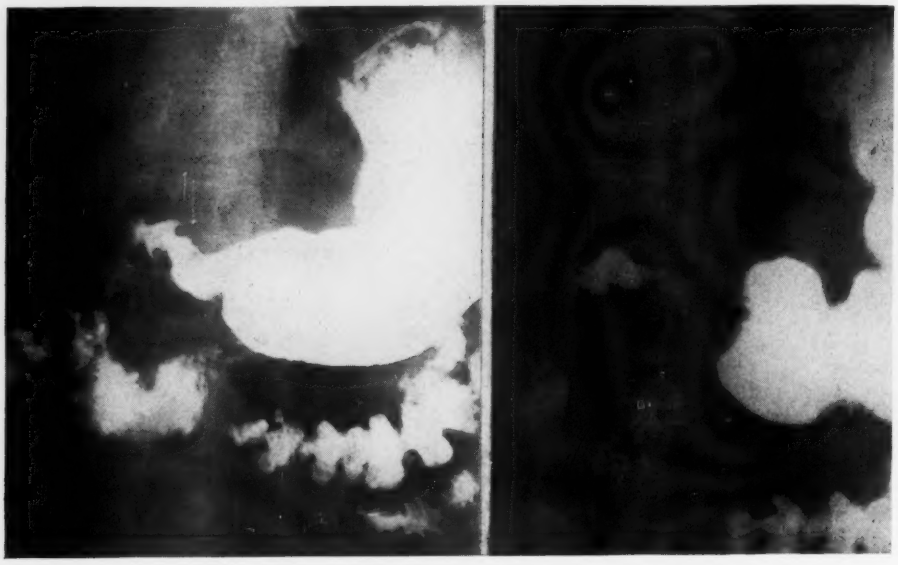


FIG. 3 FIG. 4

FIG. 3.—Case 2: Hypertrophic antral gastritis. Elongation and narrowing of antrum. Kirklin's sign present. Thickened antral folds.
FIG. 4.—Case 2: Progressive improvement six months later.

symptoms, and it is of further interest that these symptoms do not vary significantly from those cases of antral gastritis which we have seen.

Physical examination yields little information. Schindler has described a tender area to the left of the navel in some cases.[14]

Gastric acidity tends to be normal or high in cases of antral gastritis, but in antral spasm we have found that the free acid is low or absent with an ordinary test meal.

As has been mentioned, antral spasm is best estimated by the radiologist during fluoroscopy and with serial films which show the constant spasm without derangement of the normal folds of the antrum during contraction of the antrum. A detailed discussion of the mechanism of the production of these folds is without the scope of this paper. A roentgenologic diagnosis of antral

gastritis can be made during fluoroscopy in the presence of a deranged antral systole coupled with the finding of stiff unnatural folds which cannot be obliterated by pressure. The radiographs characteristically show persistent spasm with elongation and funnel-shaped narrowing of the antrum. Sometimes there is indentation of the duodenal cap said to be due to the stiffened mucosa being squeezed through the pyloric ring. This sign, "Kirklin's sign," is seen most characteristically in the type of case called pyloric stenosis[11] in adults, and which according to Stout are associated with histologic evidence of gastritis.

FIG. 5.—Case 3: Extreme hypertrophic antral gastritis, simulating carcinoma.

This extrusion of the mucosa through the pyloric ring may also be extreme in gastritis, without hypertrophy of the pylorus, and is recently reported[12] as "extrusion of the mucosa through the pyloric ring." The mucosal pattern, although enlarged and stiffened, is not usually disrupted, and the folds on relief can be seen both fluoroscopically and radiographically to run through the antrum. Even in the extreme hypertrophic forms, the complete normal architecture is not always disturbed, and the border folds of Chaoul can often be identified.

As yet no pathologic classification seems complete to cover all the types of inflammation in the antrum of the stomach seen roentgenologically, at operation, or in the pathology laboratory after gastric resection. Schindler's classification covers those seen gastroscopically and refers mainly to the changes in the mucosae as does the classification given by Vaughn,[15] in which he divides the gross pathology into three types—(1) acute edematous; (2) ulcerative;

and (3) chronic inflammatory, with hypertrophy, which he correlates with the gastroscopic pictures of—(a) reddening with edema; (b) reddening with ulceration, and chronic hypertrophic gastritis or the cobble stone appearance. Neither Schindler's or Vaughn's classification appear to include a type of hypertrophic antral gastritis of which the three cases described by Konjetzny[10] are similar to Case 3 presented in this paper. Also, the above classification seems to indicate that the process begins in the mucosa and submucosa and may spread to the deeper tissues. Particularly in the extreme hypertrophic forms it may be that the process is an interstitial gastritis, and the mucosal changes and the ulceration may be secondary.

Unexplained, also, is the relation of spasm which is always present. If an analogy holds to the rest of the gastro-intestinal tract, it may be that a disturbance in function exhibited as spasm is the underlying factor, and that the mucosal, and submucosal or interstitial inflammation or hypertrophic changes, are secondary to the spasm.

The differential diagnosis is of interest to the surgeon mainly in those cases with a defect in the antrum which simulates carcinoma. Attention to mucosa relief patterns will provide the diagnosis in many cases aided by gastroscopic examination. However, there are some cases[6] in which a definite differential diagnosis cannot be made between inflammatory infiltration of the antrum, ulceration, hypertrophic defects, and carcinoma. These doubtful cases may be observed for short periods, and with repeated examinations, but if after this brief period of observation a definite diagnosis cannot be made, then exploration should be carried out. It should be emphasized that even at operation it still may not be possible to rule out carcinoma, and even biopsy is not infallible. If any doubt as to exact nature of a lesion in the antrum exists at celiotomy, gastric resection should be done without further delay. With the present reasonably low mortality for gastric resection, delay in operation, with its risk of permitting an operable carcinoma to develop into an inoperable one, is unjustified.

CASE REPORTS

Case 1.—P. D., a 47-year-old white male, with stomach trouble for one year. Attacks of epigastric distress present for one month. Pain comes on four hours after eating. Gas on stomach troublesome. Loss of 14 lbs. weight in one year. No free acid (19 units in one hour). Roentgenologic examination: Localized prepyloric gastritis. Gastroscopic examination: Mucosa of antrum normal orange-red color. Some folds in antrum but these neither stiffened or nodular. *Diagnosis:* Antral spasm. Patient put on a bland diet and antispasmodics. One year later roentgenologic examination—normal stomach and antrum.

This is a case in which the correct diagnosis is antral spasm.

Case 2.—A. C., a 54-year-old white male, with gaseous dyspepsia for one year. Gas causes dyspnea. Distress after meals but no relation to any particular food. Acid—fasting 55/92; one hour 52/84. Roentgenologic examinations: First films showed a defect in prepyloric region which suggested carcinoma. Examination repeated in two weeks after treatment showed improvement, so further observation decided. After six

months defect had disappeared, and only spasm with thickened antral folds present. Symptoms relieved. Patient has remained well. *Diagnosis:* Antral gastritis.

This is a case of antral gastritis in which progressive improvement took place under observation.

Case 3.—T. M., a 46-year-old white male. Epigastric discomfort after meals, vomiting occasionally for one year. Anorexia and weight loss 15 lbs. one year. Severe pain on day of admission, with blood in stools. Low acid with test meal. Clinical impression: Ulcer or gastritis. Roentgenologic examination: Annular filling defect in antrum practically occluding pylorus, with appearance of new growth. Operative Findings: Large firm mass in antrum of stomach. Serosa white and infiltrated with small excrescences resembling peritoneal implants. Subpyloric and lower nodes along lesser curvature enlarged. Gross appearance resembled carcinoma, so gastric resection

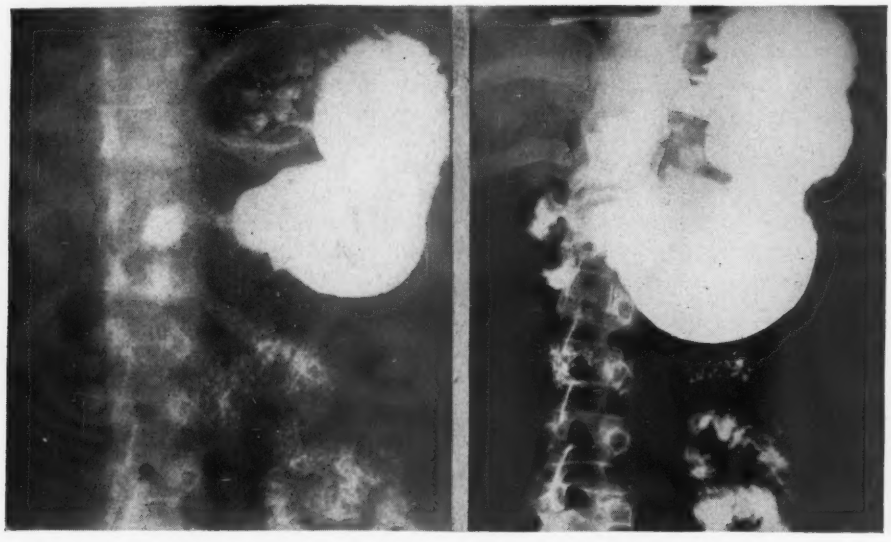


FIG. 6 FIG. 7

FIG. 6.—Case 4: Carcinoma of the pylorus simulating antral gastritis. Gastrostomy negative.
FIG. 7.—Case 4: Carcinoma of the pylorus six months later. Frozen-section negative. Paraffin section—adenocarcinoma of pylorus.

proceeded with on this basis. Anterior Pólya resection, antecolic anastomosis. Uneventful recovery.

Pathologic Report: Resected stomach. Large mass in antrum. Stomach opened shows an ulcer, ¾ inches in diameter on anterior wall near lesser curvature, three inches from pylorus. Ulcer is shallow with a necrotic base. Mucosa of antrum is red and edematous and thrown into large folds. The wall of the antrum is thickened, measuring 2 cm. The muscular coat is not interrupted and can be traced through the mass.

Microscopically: All coats show edema, with infiltration by large and small lymphocytes, plasma cells and many eosinophils. The reaction is most severe in the submucosa. There is also a diffuse fibrosis throughout the muscular layers.

This is a case of extreme hypertrophic gastritis, which by roentgenologic examination and at operation could not be distinguished from carcinoma.

Treated by gastric resection, with uneventful recovery and relief of symptoms six months after operation.

Case 4.—A. R., a 57-year-old white female. Epigastric distress of one year's duration with anorexia. Distress made worse by food. Vomiting recently. No weight loss. No free acid, but moderate amounts of free and combined acid on serial samples with ordinary test meal. Roentgenologic examination: localized prepyloric gastritis with spasm, with 25% retention in five hours. This did not improve on a short medical regimem.

Operative Findings: At the pyloric end of the stomach, and invaginating the duodenum was a rubbery induration and thickening of the antrum of the stomach. No discrete mass. Gastrotomy performed. Mucosa normal. Pylorus normal. Impression—antral gastritis. Abdomen closed.

Patient made an uneventful recovery and was well for six months, when vomiting recurred, accompanied by a small loss of weight. No anemia. Roentgenologic examination now showed prepyloric spasm with some narrowing of the pylorus. Peristalsis seen to pass through the antrum to the pylorus.

Gastroscopic Examination: Persistent spasm in the antrum. Mucosa of angulus and body of stomach normal. Pylorus not seen due to spasm.

Operative Findings: Grossly, the stomach was essentially the same as before. Gastrotomy was performed. Mucosa again appeared normal in the antrum. No ulceration. The pylorus was now narrowed and almost occluded by a ring of firm tissue. Biopsy of the pyloric ring was taken in two places. Frozen-section reported as "chronic inflammatory reaction." Because it was felt that with an apparently normal stomach with a high grade pyloric obstruction that a posterior gastro-enterostomy would be adequate to relieve her symptoms, this was done. Report on paraffin sections: Infiltrating adenocarcinoma of the pylorus. Patient made an uneventful recovery.

This is probably an early case of linitis plastica which on two occasions at operation, even with biopsy, was mistaken for antral gastritis. Resection is now contemplated due to apparent low grade of tumor without any known metastases.

CONCLUSIONS

(1) Antral spasm and antral gastritis are a fairly common cause of gastric complaints and present a not dissimilar clinical picture.

(2) Antral spasm must be differentiated from antral gastritis by roentgenologic and gastroscopic examination.

(3) Pathogenesis of antral gastritis is obscure and present classifications are incomplete.

(4) Certain types of antral gastritis are indistinguishable from carcinoma of the stomach; exploration and biopsy are not infallible and gastric resection should be undertaken unless a positive diagnosis can be made.

REFERENCES

1 Arendt, Julian: Annals of Surgery, **122**, 235, August, 1945.
2 Benedict, E. B.: Am. Jr. Roentgenol., **47**, 254, February, 1942.
3 Crohn, Burrell B.: Chronic Gastritis: Clinical Aspects. Bulletin of the New York Academy of Medicine, **15**, 293, June, 1939.
4 Forsell, G.: Am. Jr. Roentgenol., **35**, 204, February, 1936.

6 Golden, R.: J. A. M. A., **109**, 1497, November, 1937.
7 Harris, Charles M.: Am. Jr. of Surgery, **68**, 261, May, 1941.
8 Kantor, J. L.: Am. J. Roentgenol., **35**, 204, February, 1936.
9 Kirklin, B. R.: Radiology, **29**, 493, 1937.
10 Kirklin, B. R., and Harris, Milo T.: Am. Jr. Roentgenol., **29**, 437, April, 1933.
11 Konjetzny, G. E.: Der Chirug., **10**, 260, April 15, 1938.
12 McClure, C. C.: Surg., Gynec. & Obst., **52**, 945, May, 1931.
13 Norgore, Martin, and Shuler, Ivan J. D.: Surgery, **18**, 452, October, 1945.
14 Renshaw, R. J. F.: Am. Jr. Roentgenol., **47**, 254, February, 1942.
15 Schindler, Rudolph: Rocky Mountain Medical Journal, **37**, 570, August, 1940.
16 Vaughn, Walter: Radiology, **44**, 531, June, 1945.

DISPLACEMENT OF MEDIAL EPICONDYLE OF HUMERUS INTO THE ELBOW JOINT

FREDERICK M. SMITH, M.D.
NEW YORK, N. Y.

FROM THE FRACTURE SERVICE OF THE PRESBYTERIAN HOSPITAL IN NEW YORK, AND DEPARTMENT OF SURGERY, THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK, N. Y.

IT IS THE PURPOSE of this paper to review and to evaluate the results of treatment of 21 consecutive fractures (separations) of the epiphysis of the medial (internal) epicondyle of the humerus with displacement into the elbow joint treated during the period from 1931 to 1944, inclusive, on the Fracture Service of the Presbyterian Hospital, New York City. Each of these cases was either accompanied by a posterior or posterolateral dislocation of the elbow joint or had had such a dislocation reduced by a friend, another physician, or at another hospital before coming to this hospital. Each case, whether of short or long duration after injury, was treated by open operation. Of the 21 cases thus treated, 20 have been followed carefully for years, the average follow-up period being 3.45 years.

A brief discussion of the frequency of the lesion, the anatomy, mechanism of injury, clinical and roentgenologic diagnosis, ulnar nerve involvement, operative and postoperative treatment, as well as follow-up results, will also be presented.

FREQUENCY OF THE INJURY

The medial epicondyle of the humerus is very frequently injured in children. Quite the opposite is true in adults. The fact that this injury occurs mainly in childhood proves that the cartilaginous plate of the epiphysis offers but a weak attachment of the epicondyle to the medial condyle. The ossification center for this epiphysis appears on roentgenologic examination about the sixth year, and does not fuse with the diaphysis of the humerus until the 17th year.

Displacement of the medial epicondyle epiphysis into the elbow joint occurs mainly between the ages of seven to 17 years. In the series herein presented 18 of the 21 cases occurred between the ages of nine to 14 years (Table I).

In general, there are two main types of injury to the medial epicondyle epiphysis, namely, (1) mild to moderate separation of the epicondyle from the condyle; and (2) complete avulsion of the epicondyle with downward and lateral displacement and incarceration into the elbow joint. This paper purposes to deal only with the second of these two conditions.

ANATOMY AND MECHANISM OF INJURY

The medial epicondyle in its normal position lies outside of the elbow joint. The proximal attachment of the medial collateral ligament of the elbow joint is located on the lower margin of this epicondyle. From here it fans-out dis-

tally to become attached to the medial margin of the coronoid and olecranon processes and the medial margin of the greater sigmoid fossa of the ulna. Also, attached to this epicondyle is the common tendon of origin of the flexor-pronator group of muscles (pronator teres, flexor carpi radialis, palmaris longus and the humeral heads of the flexor carpi ulnaris and flexor digitorum sublimis muscles). The surface of this group of muscles is covered by a glistening white, tough fascia. Just behind the epicondyle one finds the ulnar nerve lying in a shallow groove covered with a thin layer of fascia.

The mechanism of the injury is the same as that for a posterolateral dislocation of the radius and ulna upon the humerus, *i.e.*, a fall upon the hand with the elbow completely extended. The suddenness of the violence causes hyperabduction of the forearm bones at the elbow, rupturing the medial collateral ligament or avulsing it from its attachment to the humerus below the epicondyle. At the same time, increased tension is put upon the flexor-pronator group of muscles and this, in turn, is transmitted to the medial epicondyle. Both forces acting together, *via* the ligament and the muscles, pull the epicon-

TABLE I

CASES ACCORDING TO AGE-GROUP

Age (Years)	7	8	9	10	11	12	13	14	15	16	17
Number of Cases	1	0	3	2	2	3	4	4	1	0	1

(18 cases out of 21 fall between the ages of 9 to 14 years.)

dyle epiphysis free and cause it to be displaced markedly downwards and lateralwards. If the epiphysis remains attached to the ulna by the collateral ligament, it, naturally, will tend to follow the displacement of the ulna and radius when these become dislocated. The additional factor of muscular contraction (once the epicondyle is pulled free) tends to make the displaced fragment curl laterally and downwards (Fig. 1). The glistening fascia on the surface of these muscles is unable to contract, and when the underlying muscle fibers do, the result is to turn the fragment as described above, so that in almost all cases the rounded or dome-shaped surface of the epicondyle fragment points in a proximal direction. A few exceptions to this have been noted.

In none of the cases in this series has there been a displacement of the epicondyle fragment into the elbow joint without a concurrent dislocation of both bones at the elbow joint. I do not believe the epiphyseal fragment can be sucked into the joint by a temporary vacuum produced through rupture of the medial collateral ligament and hyperabduction of the ulna on the humerus, as suggested by Patrick. In my opinion, it takes a real dislocation at the elbow with its lateral displacement, ligamentous tear and muscular contraction to draw the avulsed epicondyle into the joint. Even though the patient presents himself without an elbow dislocation, careful questioning will usually elicit the fact that the elbow was deformed immediately following the injury and that a friend or kind "helper" pulled on it, thus, reducing the original dislocation, but leaving the epicondyle within the joint.

The close proximity of the ulnar nerve, as it lies in its groove on the posterior surface of the epicondyle, explains the frequency with which partial or complete palsy of this nerve is seen following such a displacement. This may occur by one of two mechanisms, either stretching of the nerve, or more rarely by displacement of the nerve itself into the elbow joint cavity along with the displaced medial epicondyle epiphysis.

EXAMINATION

Diagnosis by clinical examination of displacement of the medial epicondyle into the elbow joint is extremely difficult, usually due to the large amount of early swelling and acute tenderness overlying the entire medial aspect of the joint. The condition may be suspected if there is obvious dislocation of both forearm bones and the usual marked prominence of the medial epicondyle cannot be palpated in its normal position on the humerus, and instead, the flattened margin of the condyle itself is felt. However, the displaced epicondyle when not felt in its normal location may have swung posteriorly (pendulum fashion) as a stripped-up periosteal attachment and not be truly in the joint cavity.

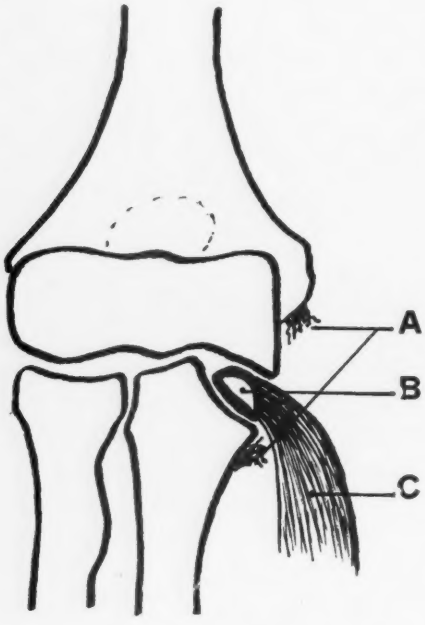


FIG. 1.—Sketch of medial epicondyle displaced into the elbow joint with attached muscles of flexor-pronator group. (A) Torn medial collateral ligament. (B) Medial epicondyle epiphysis. (C) Flexor-pronator group of muscles.

The only sure and safe way to make the diagnosis of, or rule out, medial epicondyle displacement into the joint is on roentgenologic examination. Much too frequently, however, the condition may be missed even on good roentgenograms, and not be picked-up until several weeks after the injury. The reasons for this are mainly two: (1) the physician reading the films being unaware that such a lesion can occur is consequently not on the watch for it; and (2) by mistaking the displaced epicondyle for an ossification center of the trochlear epiphysis (which may have two or occasionally three ossification centers). One should always study the films with this in view if he cannot demonstrate to his satisfaction, or is in any doubt about where the epicondyle is, he should take films of the uninjured elbow in identical positions for comparison. This may save many embarrassing moments later (Figs. 2, 3 and 4).

The lesion is not only of interest from the standpoint of accurate diagnosis, but it is extremely important to make an early diagnosis. Treatment is

obvious and should be immediate when the diagnosis is recognized; but when accurate diagnosis is not made or not recognized till late, proper treatment will either not be carried out or so late that marked impairment of function may follow.

Sometimes difficulty is encountered in obtaining satisfactory anteroposterior views on roentgenograms because of inability of the patient to fully extend the elbow. Rather than attempting to take such a view with the elbow balanced on the tip of the olecranon (which procedure causes distortion on the film of all the bones forming the elbow joint) it would be much better to take

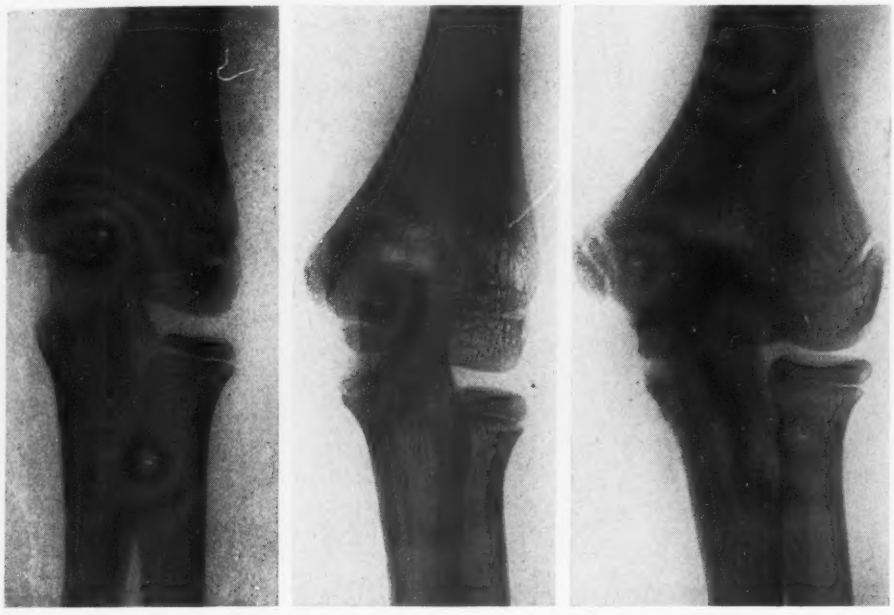


FIG. 2-A 2-B 2-C

FIG. 2.—Anteroposterior roentgenograms showing normal epihpyses of the lower humerus at (A) age 7 years; (B) age 11 years; (C) age 14 years.

two anteroposterior views—one with the lower humerus lying flat on the film and the other with the upper portion of the forearm bones lying flat on the film (Fig. 5). This would give at least one good view of the lower humerus and another of the upper ends of the radius and ulna. Usually, when the medial epicondyle is within the joint, it is situated in a position distal to the lower margin of the trochlea. On the other hand, in younger children with an incompletely ossified trochlear epiphysis where the anatomy is greatly distorted due to elbow dislocation, one must be extremely careful in studying the roentgenograms.

A very important part of the clinical examination should be to test both sensory and motor function of the ulnar nerve. Palsy of this nerve suggests such trauma as contusion or stretching. Although it should put one on his

guard in respect to a lesion of the medial epicondyle, it may occur without the medial epicondyle having been necessarily displaced into the joint. Early recognition of a nerve lesion calls for immediate operation, and possibly transplantation of the nerve, to avoid excess scar formation about it or to release tension upon it.

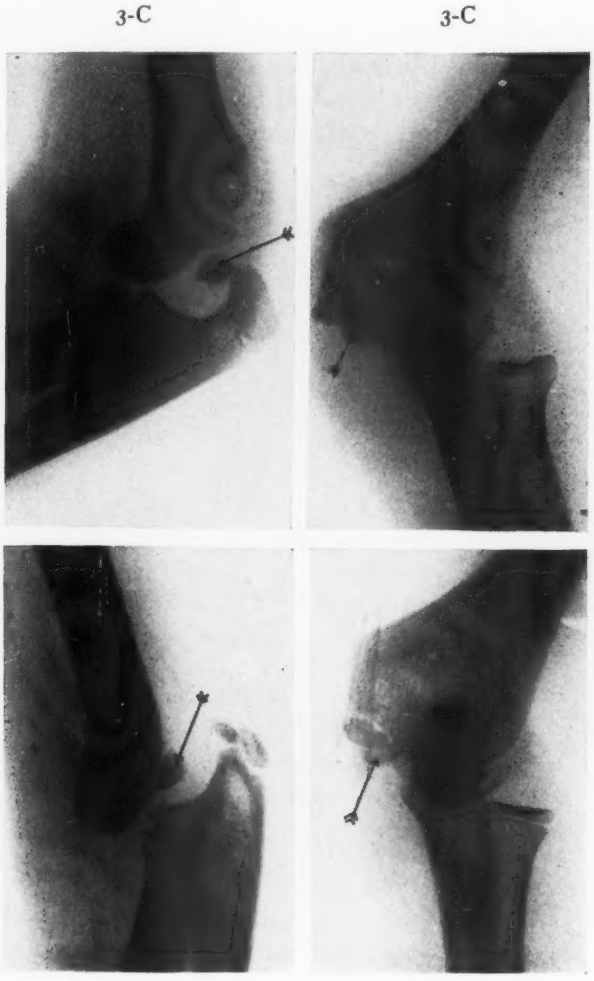
3-A 3-A

3-B 3-B

FIG. 3.—Anteroposterior and lateral roentgenograms showing the medial epicondyle epiphysis displaced into the dislocated elbow joint. (A) Case 18. (B) Case 16.

Although treatment in all of our cases has been operative for removal of the incarcerated epicondyle, and we believe this best, Schmier and Patrick have each published reports recently in which they describe conservative methods of withdrawing the epicondyle from the joint space. Schmier's method consists of extending the elbow, wrist and fingers with the forearm fully supinated while at the same time forcibly abducting the forearm at the elbow and with the thumb of the upper hand pulling distally upon the bellies of the flexor-pronator muscles. Patrick's method is very similar except that he

applies faradic current to the flexor-pronator muscles to cause these to contract violently, thereby pulling the epicondyle out of the joint. Even though either of these methods withdraws the epicondyle from the joint space, neither adequately reduces the fragment with its attached muscle mass. Consequently, no fixation of the fragment is possible and early active exercises and use cannot be insti-



3-C 3-C

3-D 3-D

FIG. 3.—(C) Case 12. (D) Case 7.

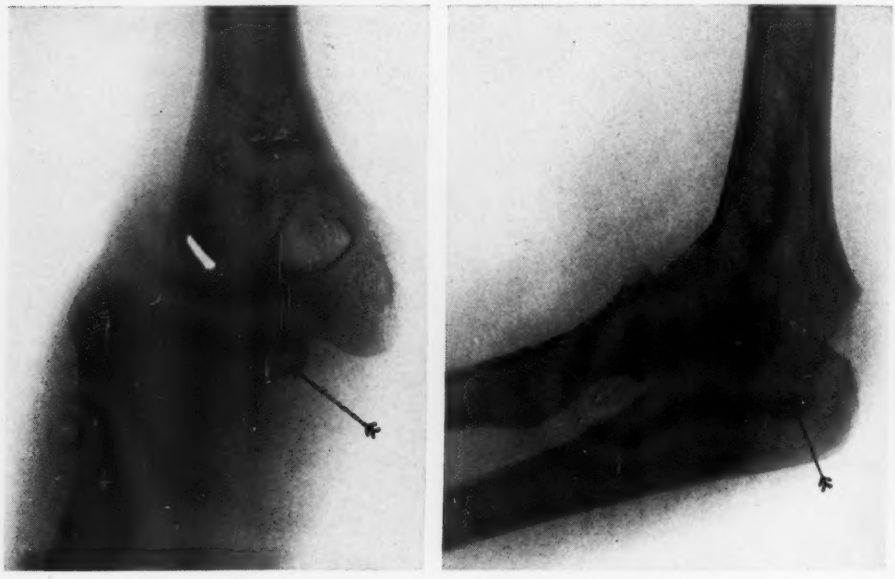
tuted and complete functional return may be impaired. Theoretically, lack of replacement or lack of excision of this epicondyle would offer greater chances of subsequent ulnar nerve palsy.

ANALYSIS OF CLINICAL CASES

This series comprises 21 cases of displacement of the medial epicondyle into the elbow joint. No comparable series, with adequate follow-up records,

has been previously published, as far as this author has been able to ascertain.

Of these 21 cases 13 came to the emergency ward within one-half to three hours following the injury. Twelve showed elbow dislocation on admission. For the past ten years we have tried to train our resident and intern staff to look for this lesion, and, consequently, nine out of the last 11 have been operated upon the day of the injury. The advantages of immediate operation from the standpoint of pathology, physiology and functional recovery are obvious and need not be discussed here. Three cases of the 21 applied for treatment on the second, third, and sixth day, respectively, after the initial injury. Three more applied after two and one-half, three and one-half, and



3-E 3-E

FIG. 3.—(E) Case 15.

four and one-half weeks, respectively. There were two cases that came to us for treatment at two and two and one-half months, respectively. It is of interest to note that of the eight "late" cases four had ulnar nerve palsies.

As previously stated, all 21 cases in this series had sustained an elbow joint dislocation. Eight of these had been reduced before coming to our clinic; two were reduced in our emergency ward; and 11 were not reduced until they reached the operating room. It was, therefore, possible to study the immediate pathology of the dislocation as well as the displacement of the medial epicondyle. In each case an extensive tear of the anterior elbow joint capsule as well as of the brachialis anticus muscle fibers was found. The medial collateral ligament was found to be ruptured in every case. In the immediate cases with ulnar nerve palsy swelling and ecchymosis were found in the nerve.

At operation, the medial aspect of the elbow joint may be exposed either through a longitudinal incision or a transverse one along the flexion crease.

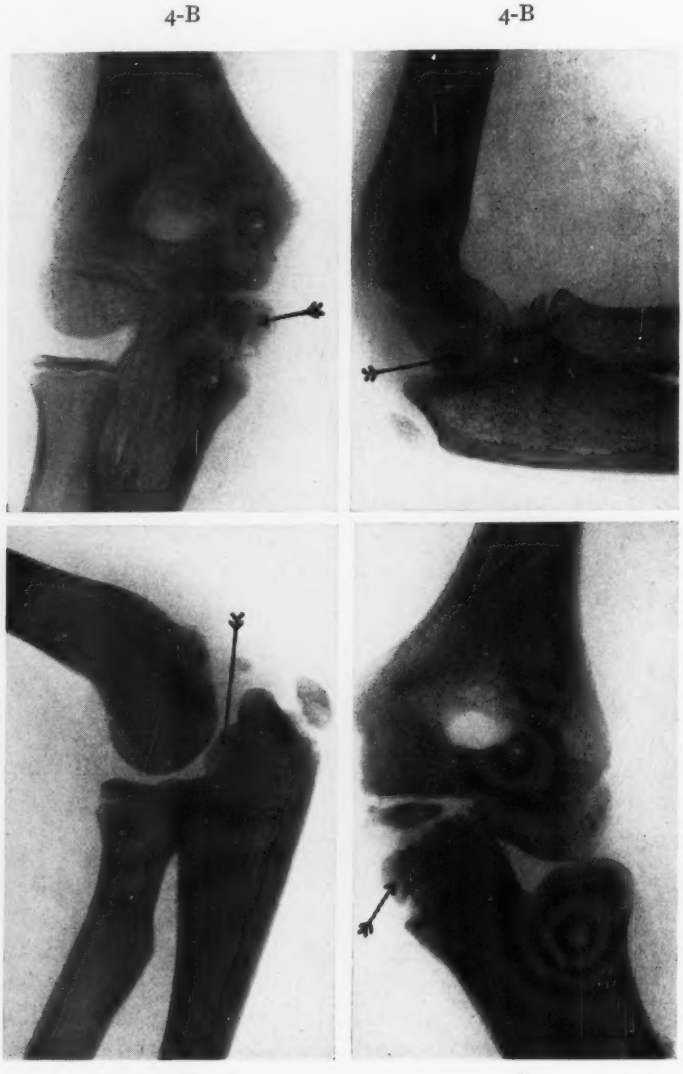
This latter incision gives a better operative scar, but is not adequate for exposure if transposition of the ulnar nerve is necessary. When the joint is exposed, the nearly circular medial aspect of the trochlear process is seen first covered by articular cartilage. Immediately below this is seen the converging fibers of the glistening white fascia overlying the surface of the flexor-pronator muscles. These fibers and muscles curl laterally into the joint cavity just distal to the trochlea. The epicondyle fragment is not seen at this time. However, if this fascia is pulled upon by a mouse-toothed forceps, the incarcerated epicondyle will "pop out" into full view. It can then be reattached to its original site or excised, according to the preference of the operating surgeon.

4-A 4-A

FIG. 4.—Anteroposterior roentgenograms showing the medial epicondyle epiphysis displaced into the reduced elbow joint. (A) Case 21.

There were seven cases associated with ulnar nerve palsy on admission (33 per cent), and one case showed a temporary palsy after operation. One of these cases with ulnar nerve palsy, an 11-year-old colored boy with sickle-cell anemia, was operated upon three days after admission and died on the table of an anesthetic death before the wound could be closed. This is the only case in the entire series that could not be followed. All cases of nerve palsy except for this death and the one postoperative palsy had the nerve treated either by injection of its sheath with saline solution and replacement of the nerve in its normal location (two cases), or by transposition of the nerve subcutaneously to the anterior surface of the medial condyle (four cases). Nerve recovery was complete in all six cases within three and one-half to eight months. In the

postoperative palsy case, the nerve showed complete recovery in two and one-half months. In one of these late cases it was found at operation that the ulnar nerve had been displaced along with the medial epicondyle and lay with it inside the elbow joint proper.



4-B 4-B

4-C 4-C

FIG. 4.—(B) Case 10. (C) Case 6.

Treatment of the medial epicondyle *per se* after extraction from the joint and after reduction of the elbow joint (if unreduced) consisted in fastening it to the medial condylar ridge by means of a suture of heavy silk passed through a drill hole in the ridge in 15 cases. In one case, a 17-year-old boy, it was

replaced and fastened with a single stainless steel screw. In five cases the epicondyle was completely excised and the common tendon of origin of the flexor-pronator group of muscles was resutured to the medial condyle with heavy silk. Whether the epicondyle should be replaced and sutured or whether it should be excised and the muscles resutured offers a chance for some interesting speculation. Inasmuch as it was removed in but five cases in this series, and two of these were of over two months' duration, it is difficult to lay down any rules in respect to replacement or excision of the fragment (Fig. 6). It is my impression, however, that by removal in early cases, a quicker return of elbow joint function may possibly be expected provided that postoperative splinting is not carried out longer than two weeks. The irregularity that often

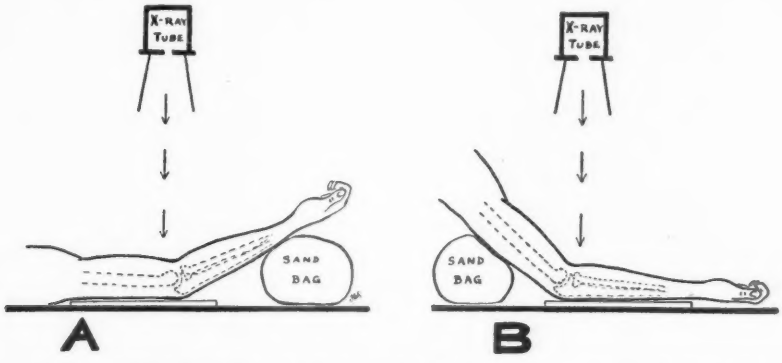
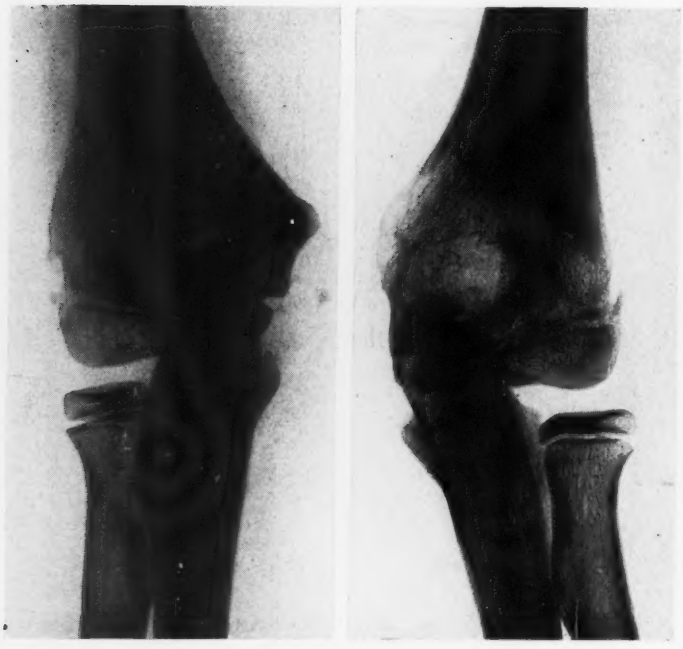


FIG. 5.—Sketch demonstrating method of taking anteroposterior views of a bent elbow in order to prevent distortion. (A) Position with humerus on the film. (B) Position with radius and ulna on the film.

takes place (from growth disturbance) following injury to, and replacement of, the epicondyle, plus the fact that 26.7 per cent reunited only by fibrous union would theoretically be a reason for removing it at operation. On the other hand, it is quite evident that in the cases in which the epicondyle was replaced (whether the epicondyle developed slight irregularity or enlargement) not a single case developed any late ulnar nerve disturbance or loss of function that could be attributed to the epicondyle *per se*. Actually, from the viewpoint of function I believe it makes very little difference whether the epicondyle is replaced or removed.

The only other reason for excision of the epicondyle fragment in addition to those mentioned above would be a purely cosmetic one. Late clinical follow-up examinations show slight to moderate enlargement of the epicondyle on palpation when carefully compared to the uninjured elbow. Occasionally it is found to be slightly sharper in outline if not enlarged (Figs. 7 and 8). In either case, however, the patient or his parents are usually unaware of any of these variations in the anatomy. Although follow-up roentgenograms show somewhat more irregularity and enlargement of the epicondyle than can be



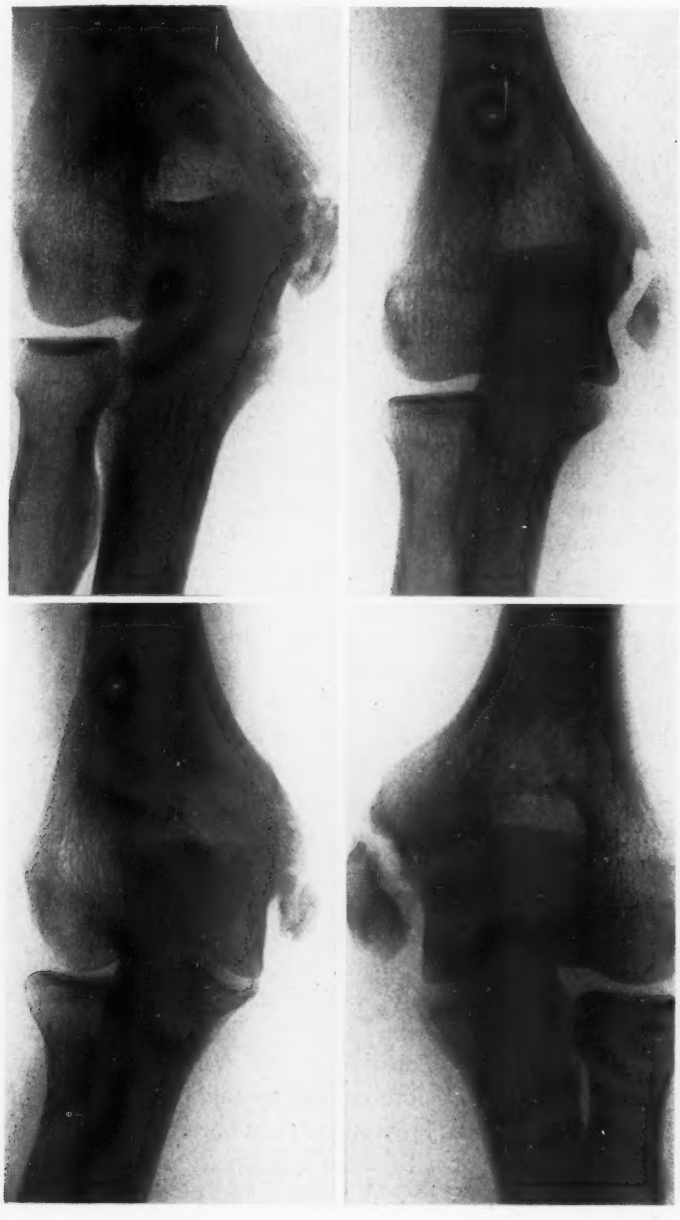
6-A 6-B

FIG. 6.—Follow-up anteroposterior roentgenograms of cases in which the medial epicondyle was excised at operation. (A) Case 19, 6 months after operation. (B) Case 21, 1 year and 4 months after operation.

7-A 7-B

FIG. 7.—Follow-up anteroposterior roentgenograms showing bony union of the medial epicondyle to the condyle with irregularity of the former. (A) Case 14, 1 year and 5 months after operation. (B) Case 12, 1 year after operation.

8-A 8-B



8-C 8-D

FIG. 8.—Follow-up anteroposterior roentgenograms showing fibrous union of epicondyle and irregularity. (A) Case 18, 10 months after operation. (B) Case 16, 10 months after operation. (C) Case 11, 6 years after operation. (D) Case 6, 1 year and 8 months after operation.

noted clinically, this at present would appear to be a poor reason for deciding to excise the epicondyle in all subsequent cases in which operation is to be performed.

The most important single factor in the rapidity and completeness of return of function is the length of time that the elbow is kept immobilized after operation. The cases that did best early, and have continued to do so, are those that were immobilized in a posterior moulded plaster splint for *less than two weeks after operation* or had only a sling following operation.

FOLLOW-UP RESULTS

There have been 21 cases of this type operated upon during the last 13 years, of which 20 have been followed for an average follow-up period of 3.45 years. The longest follow-up period was eight years and nine months, and the shortest was 9.5 months. This latter case could not be followed longer owing to the fact that the patient moved to California. Her result at the time of her last follow-up visit was excellent and the only defect she showed was 10° loss of complete extension at the elbow.

In general, it can be said that the follow-up period has been adequate and that the results quoted are as close to end-results as could possibly be made. All follow-up results have been based on careful clinical evaluation of the patient's extremity and not by letter. These examinations have been very stringent and particular care has been taken to search for any residual defect rather than making the examination purely superficial. Only those patients having a result that could be considered perfect from the standpoint of residual anatomic deformity, function, or economic loss, have been given a rating of "4" in the follow-up of each of these categories. Any patient with a result less than 100 per cent perfect in any of these categories has been given a follow-up rating of "3" or less (Table II).

On summing up the ratings of the various patients it may be said that six have obtained completely perfect results; four have excellent results (this group is made up of cases in which a very slight prominence or irregularity of the medial epicondyle was the only abnormality); nine have received what might be considered good to excellent results, the majority of these showing slight limitation of elbow flexion or extension. One case received what could be considered a fair to good result (Case 5). This case had been previously operated upon, but without the medial epicondyle having been removed from the elbow joint two months before coming to this clinic. None of the cases followed showed any economic loss. In children our evaluation of the economic rating is based on whether or not the child can carry on his usual school activities and activities in sports, *etc.* A good many of these have subsequently finished school and have secured occupations without finding any handicap from the standpoint of the elbow.

In addition to clinical evaluation of the follow-up results of these cases, late roentgenologic examinations have also been made. It is interesting to note that of the 15 followed cases in which the medial epicondyle was replaced at oper-

TABLE II

TABLE II.

CASE NO.	AGE	TIME AFTER INJURY (0 = SAME DAY)	ELBOW DISLOC REDUCED AT: OUTSIDE	EMERGENCY WD.	AT OPERATION	ULNAR NERVE PALSY	TIME BETWEEN ADMISSION & OPER. IN DAYS	FIXATION OF MEDIAL EPICONDYLE	TREATMENT OF ULNAR NERVE	POST-OPERATIVE SPLINTING	OFF TREATMENT AT	ULNAR N. RECOVERY AT	FOLLOW-UP: TIME AFTER OPERATION	RATING: ANATOMIC	RATING: FUNCTIONAL	RATING: ECONOMIC	REMARKS
																	ANATOMIC "3" = SLIGHT ENLARGMENT OF MEDIAL EPICONDYLE. MOTION RANGES ARE NORMAL UNLESS SPECIFICALLY INDICATED BELOW.
1	9	4½ WKS.	+			0	7	SILK		2 WKS.	5½ WKS.		8¾ YRS.	3	3	4	ELBOW RANGE 55-150°
2	11	0			+	+	3	SILK	?								DIED. ANESTHETIC DEATH.
3	14	2 DA.	+			+ POP	1	SILK		SLING ONLY	2¼ MOS.	2½ MOS.	4¼ YRS.	4	4	4	POST-OP. NERVE PALSY. FULL RECOVERY IN 2½ MOS.
4	13	0		+		0	3	SILK		8 DAYS	2½ MOS.		2⅜ YRS.	4	4	4	
5	15	9 WKS.	+		+	0	7	EPICONDYLE EXCISED		3 WKS.	7 WKS.		2¼ YRS.	3	2	4	PRIOR OP. EPICONDYLE LEFT IN JOINT. REMOVED AT OP. HERE VIA TRANS-OLECRANON APPROACH. ELBOW RANGE 50-115° PRONATION ⅘. BONY BLOCK TO EXTENSION. FULL USE.
6	13	3 DA.	+			0	1	SILK		SLING ONLY	7 WKS.		1⅔ YRS.	3	4	4	
7	12	0			+	0	0	SILK		2 WKS.	8 WKS.		4 YRS.	3	3	4	ELBOW RANGE 40-180°. PRONATION ¾.
8	9	0			+	0	1	SILK		1 MO.	2¼ MOS.		10 MOS.	4	3	4	ELBOW EXTENSION LIMITED 10°. MOVED TO CALIFORNIA.
9	9	3½ WKS.			+	+	6	SILK	REPLACED. INJECTED WITH SALINE	5 DAYS	2¼ MOS.	5 MOS.	5 YRS. 1 MO.	3	3	4	NERVE FOUND IN JOINT. PRONATION ⅘. FLEXION LIMITED 10°. ULNAR NERVE RECOVERY COMPLETE.
10	11	0	+			0	0	SILK		18 DAYS	6½ WKS.		4¼ YRS.	3	4	4	
11	12	2½ WKS.	+			+	2	SILK	TRANPOSED	SLING ONLY	3 MOS.	5 MOS.	6 YRS.	4	4	4	ULNAR NERVE RECOVERY COMPLETE.
12	13	0			+	0	0	SILK		9 DAYS	2 MOS.		5⅓ YRS.	3	3	4	ELBOW EXTENSION LIMITED 10°. SLIGHT WEATHER ACHE.
13	17	6 DA.	+			+	3	1 SCREW	TRANSPOSED	3 WKS.	4½ MOS.	3½ MOS.	3¼ YRS.	3	3	4	ELBOW EXTENSION LIMITED 20°. ULNAR NERVE RECOVERY COMPLETE.
14	14	0			+	0	0	SILK		8	2		3¼	3	4	4	
15	12	0	+			+	0	SILK	REPLACED. INJECTED WITH SALINE.	13 DAYS	7 WKS.	8 MOS.	2⅔ YRS.	4	4	4	ULNAR NERVE RECOVERY COMPLETE.
16	13	0			+	0	0	SILK		SLING ONLY	6½ WKS.		3¼ YRS.	4	4	4	
17	7			+		0	0	EPICONDYLE EXCISED		4 WKS.	4½ WKS.		2¾ YRS.	3	3	4	ELBOW FLEXION LIMITED 25°.
18	14	0			+	0	0	SILK		8 DAYS	3 MOS.		2½ YRS.	3	3	4	ELBOW EXTENSION LIMITED 5°.
19	10	0			+	0	0	EPICONDYLE EXCISED		13 DAYS	3 MOS.		2⅓ YRS.	4	4	4	
20	14	0	+			+	1	EPICONDYLE EXCISED	TRANSPOSED	SLING ONLY	4½ MOS.	8½ MOS.	1 YR.	3	3	4	ULNAR NERVE RECOVERY COMPLETE. OCCASIONAL MILD PAIN ALONG NERVE.
21	10	10½ WKS.	+			+	5 WKS.	EPICONDYLE EXCISED	TRANSPOSED	13 DAYS	5 WKS.	4½ MOS.	1⅓ YRS.	3	4	4	ULNAR NERVE RECOVERY COMPLETE.

ation and fastened with a silk suture or a screw, 11 of these reunited to the diaphysis of the humerus by bony union (73.3 per cent). This is a somewhat higher percentage of bony union of the epicondyle than is generally supposed to take place after such an injury.

SUMMARY

1. Twenty-one cases of separation of the medial epicondyle of the humerus with displacement into the elbow joint have been reported. All of these cases have been operated upon and all have been followed for an average of over three years, with the exception of one case.

2. Each case of separation of the medial epicondyle with displacement into the elbow joint has been associated with a dislocation of both bones at the elbow joint.

3. The only anatomic deformity detected clinically on late follow-up examinations of these cases is some slight enlargement or irregularity of the medial epicondyle, which in all instances has remained undetected by the patient himself.

4. Bony union of the replaced medial epicondyle as determined by follow-up roentgenologic examination took place in 73.3 per cent of these cases.

5. No late cases of ulnar nerve palsy developed regardless of whether the medial epicondyle was replaced and subsequently healed by fibrous or bony union or with any enlargement or irregularity. Therefore, we feel that the fear of late ulnar nerve palsy which may result from possible growth disturbance in the epicondyle has been greatly exaggerated.

6. All cases associated with ulnar nerve palsy recovered complete function of this nerve.

7. The only symptomatic complaint of any of the followed cases was an occasional instance of slight bad-weather ache. The functional loss of elbow motion was practically minimal, being a limitation of 10° to 15° of flexion or extension in those cases which showed any loss at all. In only two cases was there any greater loss and these were both late cases. However, this loss of function did not interfere in any way with the patient's use or his activities in sports.

8. From the economic standpoint every patient followed showed complete use of the elbow without any handicap whatsoever.

REFERENCES

[1] Aitken, A. P., and Childress, H. M.: Intra-articular Displacement of the Internal Epicondyle Following Dislocation. Jour. Bone & Joint Surg., **20**, 161, 1938.

[2] Bancroft and Murray: Surgical Treatment of the Motor Skeletal System. Chap. 31, J. B. Lippincott, Phila., 1945.

[3] Bonin, J. G.: A Complete Outline of Fractures. William Heineman (Medical Books), Ltd., London, 1941.

[4] Boyd, H. B., and Altenberg, A. R.: Fractures about the Elbow in Children. Arch. of Surg., **49**, 213, 1944.

[5] Cotton, F. J.: Elbow Dislocations and Ulnar Nerve Injury. Jour. Bone & Joint Surg., **11**, 348, 1929.

[6] Dunlop, J.: Traumatic Separation of the Medial Epicondyle of the Humerus in Adolescence. Jour. of Bone & Joint Surg., **17**, 577, 1935.

[7] Higgs, S. L.: Fractures of the Internal Epicondyle of the Humerus. Brit. Med. Jour., July-Dec., 1936, p. 666.

[8] Patrick, J.: Fracture of the Medial Epicondyle with Displacement into the Elbow Joint. Jour. of Bone & Joint Surg., **28**, 143, 1946.

[9] Schmier, A. A.: Fracture-dislocation of the Elbow with Ulnar Nerve Involvement. Jour. of Bone & Joint Surg., **18**, 1030, 1936.

[10] *Idem:* Fracture-dislocation of the Elbow with Displacement of the Internal Epicondyle into the Joint. Amer. Jour. of Surg., New Ser., **45**, 116, 1939.

[11] *Idem:* The Internal Epicondyle Epiphysis and Elbow Injuries. Surg., Gynec. & Obst., **80**, 416, 1945.

[12] Watson-Jones, R.: Fractures and other Bone and Joint Injuries. Williams and Wilkins Co., Baltimore, 1940.

[13] Wilson, P. E.: Fractures and Dislocations in the Region of the Elbow. Surg., Gynec. & Obst., **56**, 335, 1933.

A TECHNIC FOR COMBINED MEASUREMENT OF MOTILITY AND ELECTRIC ACTION POTENTIALS IN THE HUMAN INTESTINE

J. Roy Smith, Ph.D., M.D.

WITH THE TECHNICAL ASSISTANCE OF CHARLES MARKEY

New York, N. Y.

FROM THE SURGICAL SERVICE OF THE PRESBYTERIAN HOSPITAL, NEW YORK, N. Y.

The Miller-Abbott tube, aside from its multiple uses as a therapeutic and diagnostic instrument, may be used as a convenient means of measuring intestinal motility by connecting its inflated balloon to a recording manometer. Like other similar arrangements this technic is subject to certain known limitations recently detailed by Brody, *et al.*[1] Important among these is the fact that pressure variations so recorded bear no constant relation to true intraluminal pressure changes (Abbott, *et al.*[2]). However, the balloon-manometer method does give empirically reproducible patterns of motility and such measurements, in the intact and in the sick bowel, in conjunction with clinical and roentgenographic data, add considerably to a better understanding of the dynamics of physiologic dysfunction in ileus and other disturbances of motility (Ingelfinger and Abbott[3]). Study of the electrical action potentials of the intestinal wall provides a supplementary dimension of information which may well repay exploitation. In line with the established status of the electrocardiogram and the practical clinical evolution of the electro-encephalogram it appears reasonable to assume that the mural electrogram of the intestine should emerge eventually as a useful adjunct to the other technics now available for the study of intestinal disease. Forster, *et al.*,[4] recently described action potentials recorded from the intact human intestine in conjunction with contractile activity, with particular reference to their legitimacy and their relation to known features of smooth muscle action potential patterns. The present paper outlines a technic for the practical clinical measurement of the intestinal electrogram with simultaneous recording of intestinal motility, built around the Miller-Abbott tube.

MEASUREMENT OF INTESTINAL MOTILITY

In our apparatus for recording intestinal motility, pressure variations inside the Miller-Abbott tube balloon deflect a mercury column which interrupts a light beam incident upon a photo-electric cell producing alterations of electrical potential which are amplified to activate an ink-writing oscillograph. Details of the amplifier circuit and the manometer photo-electric cell arrangement are shown diagrammatically in Figure 1-a.

The light beam traverses one limb of the manometer and passes through a slot in the wall of a light-tight metal container which houses the photo-electric cell. The slot, ten mm. long by five mm. wide, is centered with respect to the light beam and the element of the cell. The manometer, made of six-mm. bore

glass tubing, is adjustable in a vertical direction and rides snugly in front of the slot in a channel formed by two pieces of felt bordering the slot on either side. Each limb of the manometer is flanked on corresponding sides by a metal millimeter scale visible through a peep-hole in the front wall of the metal case containing the unit and permitting moment-to-moment notation of pressures.

The manometer limb traversing the light beam is connected with the Miller-Abbott tube *via* a length of pressure rubber tubing and a T-tube. In practice, enough air is injected to inflate the balloon fully without distention (25–30 cc.), and the manometer is then adjusted so that the midpoint of the slot bisects (approximately) the current excursions. Adjustment of the amplifier output balance control (Fig. 1-a) similarly permits the excursions of the recording pen to be centered over its mid or neutral position and the observation proceeds.

The recording unit is a cinaudograph oscillograph with an over-all pen excursion of three cm., which writes on a motor-driven paper tape moving 28 mm. per minute. The entire apparatus is mounted on a portable table which is wheeled to the patient's bedside for the recording. The amplifier provides a stable baseline without drift and, considering the very slow frequencies of intraluminal pressure change in the intestine, meets the necessary criterion of passing direct current. The over-all amplitude response, moreover, is linear for manometer deflections within the bounds of the ten mm. light slot which encompasses the usual range of excursion as we have observed it to date with this apparatus.

Some 50 exploratory observations have been made using this apparatus. Aside from studies on five "normal" patients (no gastro-intestinal history) and a case of tropical sprue who were intubated for the purpose, recordings ordinarily were made during the course of diagnostic or therapeutic Miller-Abbott intubations on the surgical services of the Presbyterian Hospital. A few sample records are presented in Figure 2 to indicate the scope of the pattern spectrum encountered. While these observations do not merit detailed discussion in clinical context at the present time, certain general features and clinical correlations are of interest. Rhythmic fast waves at 8–12 per minute may dominate the patterns observed in the normal small bowel (Fig. 2-a) but are usually seen in conjunction with slower waves at 1–1.5 per minute (Figs. 2-c, 2-d). Occasionally, large slow irregular one per minute waves take complete precedence (Fig. 2-b). In paralytic ileus, large dispersed slow components at 0.5–1.0 per minute appear against a baseline background (Fig. 2-e). As seen in one patient (Fig. 2-f) these waves gave way dramatically to a "normal" rhythm at 8–12 per minute accompanying an overnight decompression of a severe inhibitive ileus following drainage of an appendiceal abscess (Fig. 2-g). In harmony with the recent findings of Ingelfinger and Moss,[5] a case of tropical sprue, prior to treatment gave consistent baseline jejunal patterns (Fig. 2-h). Seven weeks later, after dietary and vitamin therapy and marked clinical improvement, the characteristic "normal" pattern of alternating slow and fast rhythmic waves had appeared (Fig. 2-i). Respiratory arti-

facts are occasionally observed (Figs. 2-f and i) and rarely are fairly prominent (Fig. 2-e).

COMBINED MEASUREMENT OF MOTILITY AND ACTION POTENTIALS

Available methods for recording action potentials from the intact intestine suffer by comparison with the precise technics developed to record electrophysiologic phenomena in other tissues. Observations must be made by remote management with no direct control over the critical factors of electrode placement and contact and with the electrodes bathed in an electrolytic fluid medium which, on theoretic grounds, might well be calculated to produce polarization artifacts. On practical grounds these difficulties are resolved in the empirical demonstration that bonafide electrical action potentials can be recorded from electrodes held in position against the intestinal wall by a balloon, as demonstrated earlier by Forster, *et al.*,[4] and the problem becomes one of devising a suitable electrode bearing balloon.

Our aim was to record action potentials bipolarly from the intestinal wall. The balloon-electrode arrangement we are using at present, and which has proven fairly satisfactory, is shown in Figure 1-b. The electrodes are three-mm. lead disks soldered to lengths of No. 34 enamelled copper wire. The terminal two cm. of wire with the electrode at its tip is attached by rubber cement to the outer surface of the condom rubber balloon. Four electrodes are held in place in this manner at intervals of approximately 1.5 cm. around the mid-circumference of the inflated balloon. The balloon is so constructed, by decreasing the length of condom rubber tubing used, that when collapsed it forms a pleated sleeve around the terminal four cm. of tube proximal to the perforated metal tip rather than a redundant bag. This facilitates passage of the tube tip through the nose with little discomfort to the patient and with minimal electrode mortality. A correlate of this arrangement is the addition of a definite increment to the recorded intraluminal pressure due to the elastic tension of

---

FIG. 1-a.—The amplifier circuit and photo-cell manometer arrangement. The amplifier is amplitude modulated, employs the 60 cycle power frequency as a carrier and is equivalent to a D.C. amplifier. Its upper frequency limit is approximately seven cycles per second. The photo-electric cell is in a bridge circuit. Adjustment of the balance control in this circuit varies the negative bias of the control grid No. 1 of the 6L7 tube and hence the amount of current through this tube which in turn varies the amplitude of the 60 cycle carrier. This carrier level is impressed on the push-pull grids of the 6L6's output stage after rectification and appears as a direct current through the oscillograph. The amount of deflection of the pen will depend on the height of the carrier amplitude and a steady deflection of the pen will occur if the carrier level remains unchanged. Hence the balance control can adjust the zero pen deflection. A change in the intensity of the light incident on the photo-cell due to variation of the mercury level in the light beam causes the resistance of the cell element to change and unbalances the bridge circuit which in turn varies the grid bias of control grid No. 1 of the 6L7 and deflects the oscillograph pen.

FIG 1-b.—The electrode-bearing tube tip with balloon collapsed and inflated.

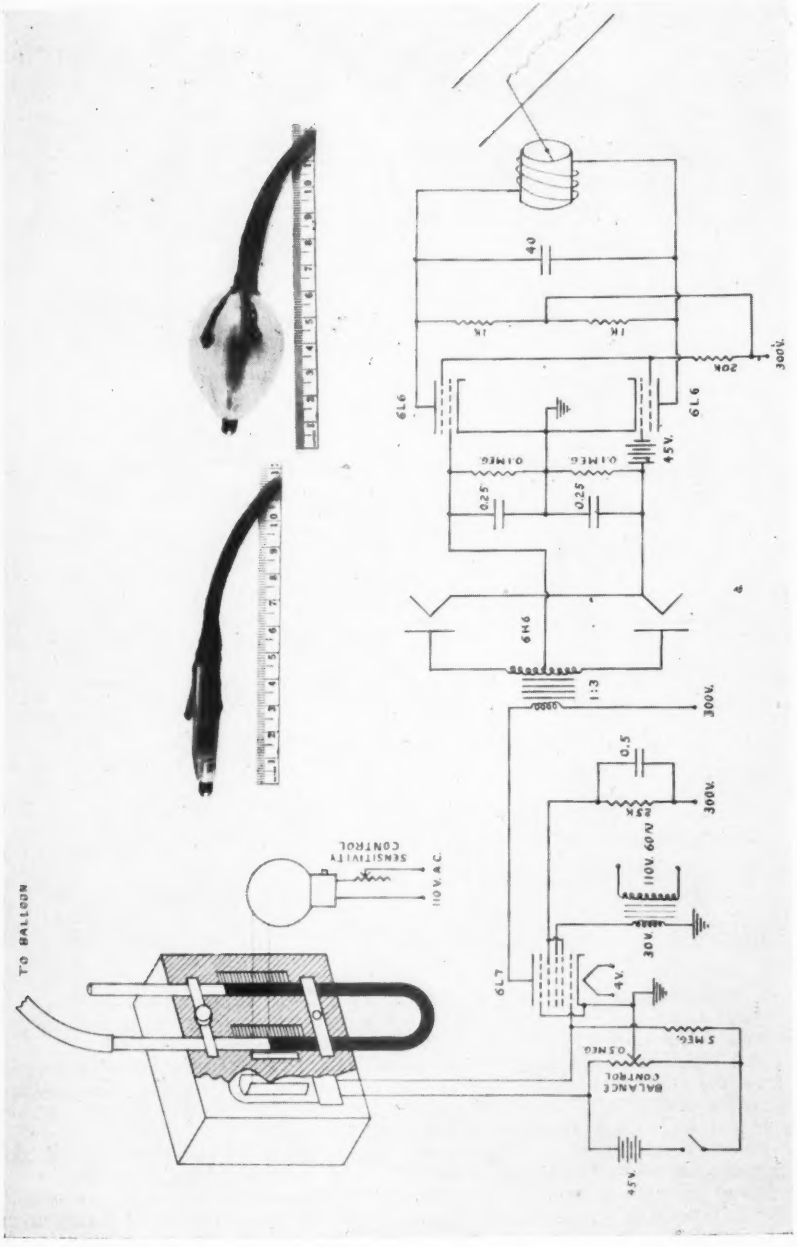

TO BALLOON
SENSITIVITY CONTROL
110 V. A.C.
6L7
4V.
30V.
110V. 60 V
300V.
6H6
6L6
45V.
BALANCE CONTROL
0.5 MEG.
0.5 MEG.
0.25
0.25
0.1 MEG.
0.1 MEG.
1 M
1 M
20K
300K
40
0.5
1:3

FIG. 1

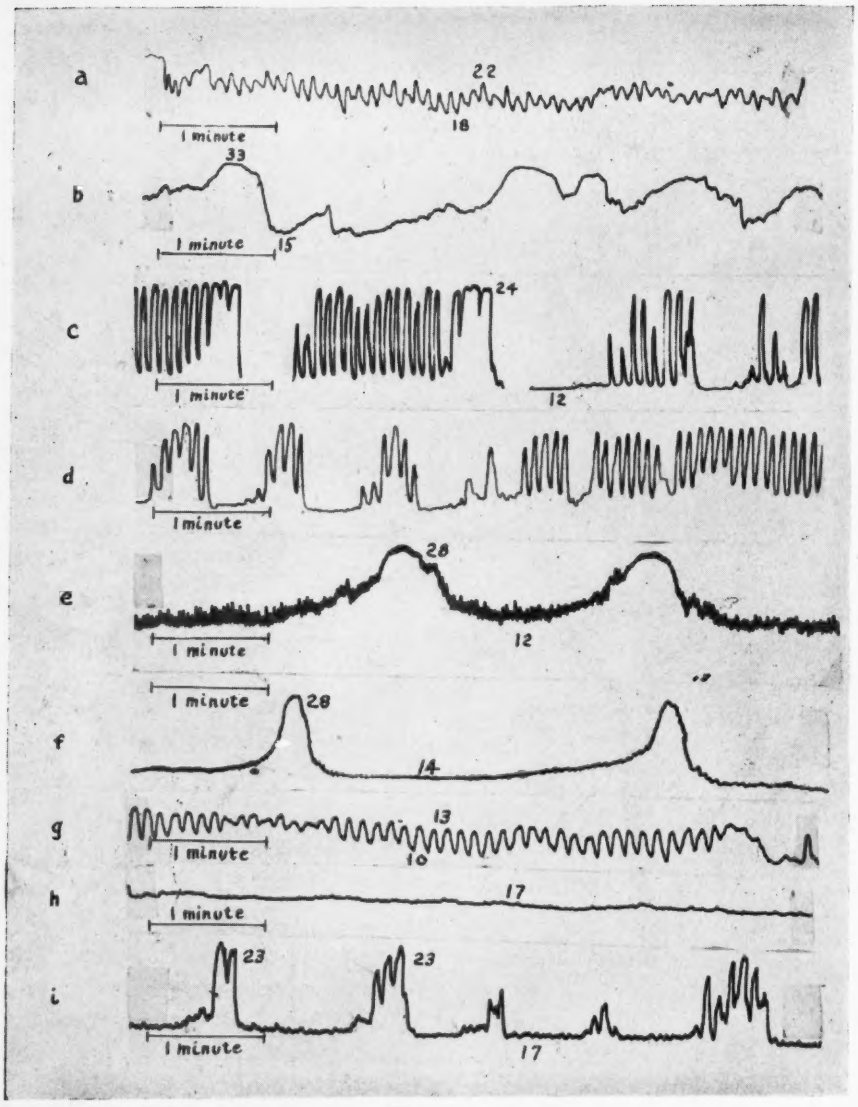


FIG. 2

FIG. 2.—Sample motility patterns from various levels in the small intestine. The numbers above and below the tracings indicate the manometer pressures in millimeters of mercury recorded at the corresponding times.

(a, b, c) Tracings from three "normal" subjects (no gastro-intestinal history), a: Duodenum—typical rhythmic fast waves at 8-12 per minute. b: Proximal jejunum—irregular large slow waves. c: Proximal jejunum—dominant fast rhythm at ten per minute alternating with large slow waves at 1.5 per minute.

(d) Proximal duodenum—similar normal pattern observed two days after ileocolectomy for carcinoma of cecum; abdomen flat, soft, with normal peristaltic sounds.

(e) Distal jejunum—dispersed abnormal large slow components seen in severe postoperative paralytic ileus (acute salpingitis, pelvic peritonitis). The small waves are respiratory artifacts.

(f) Midileum—similar abnormal pattern in paralytic ileus 48 hours after drainage of appendiceal abscess.

(g) Midileum—same patient 24 hours later, after decompression by Miller-Abbott tube. Rhythmic fast waves as seen in normal intestine.

(h) Upper jejunum—abnormal baseline pattern observed in case of tropical sprue early in course of dietary and vitamin therapy.

(i) Upper jejunum—same patient seven weeks later, after marked clinical improvement. "Normal" pattern with typical fast (8–12 per minute) and slow (1–1½ per minute) waves. Small respiratory artifact.

the inflated balloon which under our conditions (20 cc. air) amounts to approximately five mm. of mercury but which does not qualitatively change the motility patterns. In order to stiffen the balloon tip which under these conditions tends to buckle when inflated, a coil of No. 20 steel wire is placed sleeve-fashion around the segment of tube inside the balloon.

The four leads from the balloon are gathered together at its proximal end and under a collar of rubber cement sealing the balloon attachment at this end pass into the air conduit of the double-lumined tube. At the proximal end of the tube the air conduit is attached to a glass Y-tube mounted on a small bakelite panel. The four leads pass through one limb of the Y and thence through a section of rubber tubing which is sealed air-tight around them by a bar screwed over the tube to the panel. Each lead is soldered to an appropriately marked terminal mounted on the panel. The other limb of the Y is connected to a short length of rubber tubing through which the balloon is inflated. The second lumen of the tube, which serves for aspiration or introduction of material into the intestine, is connected at the panel to a short length of rubber tubing to accommodate a 20-cc. syringe.

The intestinal action potentials were recorded on a three channel portable electro-encephalograph in which condenser coupled amplifiers of push-pull input design activate cinaudograph ink-writing oscillographs.* In practice, potentials were recorded on one or two channels and intestinal motility on the third. In order to delineate the detail of the potentials which have considerably higher frequencies than the motility waves, recordings were made at a tape speed of 15 mm. per second. At this speed the slower intraluminal pressure variations are considerably spread out on the record. Visualization of the individual motility waves in their over-all pattern context was facilitated by recording them simultaneously with a separate oscillograph on the slower tape at 28 mm. per minute.

Combined recordings of intestinal motility and action potentials have been made on five patients. Three patients were intubated with the electrode-bearing tube and observations were made at various positions in the proximal small intestine. In each of the other two patients recordings were obtained from the distal colon by inserting the tube into a permanent colostomy.

One's first concern is with the legitimacy of the patterns recorded from electrodes held in contact with the intestinal wall by the Miller-Abbott tube balloon as valid reproductions of electrical discharge originating in the mural tissues. Two signal features of intestinal action potentials emphasized earlier[4] testify as to their validity and have been consistently verified in our observations. These are: (1) the appearance of the potentials before the onset of contractile activity in the intestine; and, conversely, (2) the defervescence of the electrical discharge prior to the cessation of mechanical activity (cf. especially Figs.

* We are indebted to Dr. Paul Hoefer of the Department of Neurology, College of Physicians and Surgeons, who very kindly loaned this equipment to us for these observations.

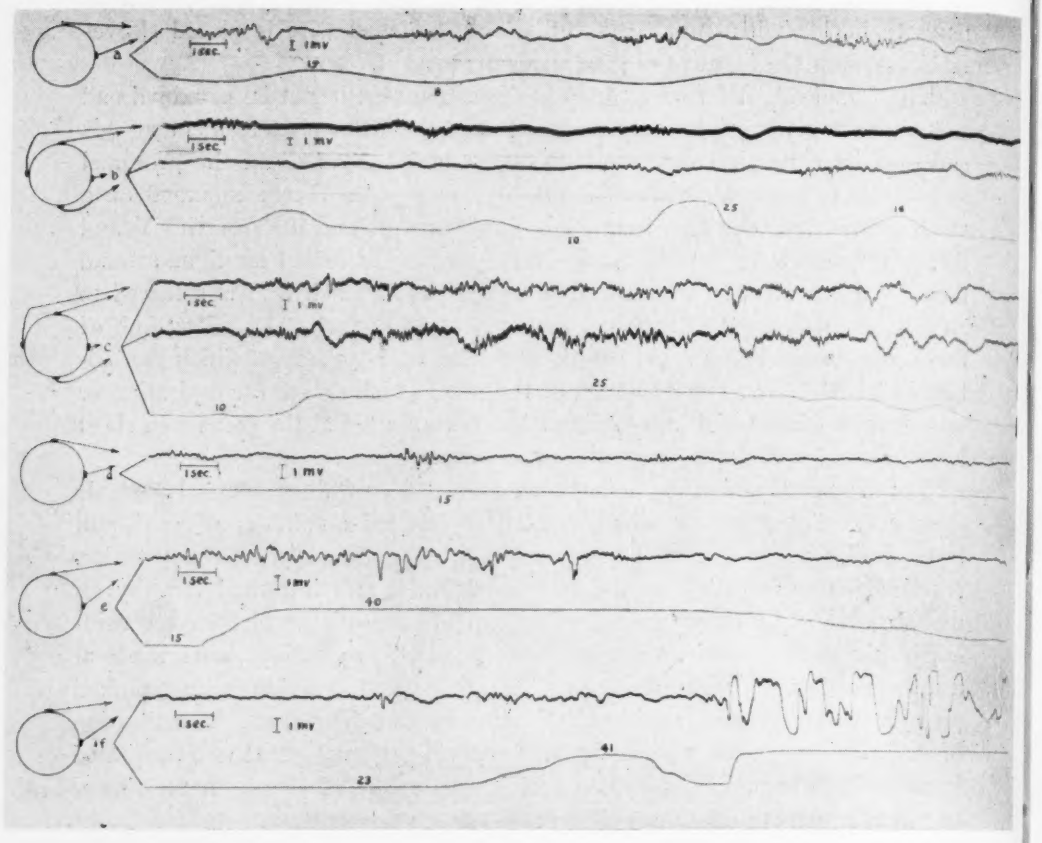


FIG. 3

FIG. 3.—Combined tracings of electrical action potentials and intestinal motility. Electrode arrangement indicated by diagram at left of each set of tracings depicting balloon in cross-section. The numbers above and below the motility record (lower tracing in each instance) indicate manometer pressures in millimeters of mercury.

(a) Proximal jejunum—potentials associated with rhythmic waves at ten per minute. Normal subject.

(b) Similar motility rhythm and potential patterns from duodenum. Carcinomatosis (liver metastases) secondary to carcinoma of transverse colon; chronic pancreatitis.

(c) Proximal jejunum—potentials accompanying slower intestinal contraction. Catarrhal jaundice.

(d, e, f) Sigmoid colon—balloon inserted six inches into permanent colostomy.

(d) Rhythmic electrical discharges in absence of detectable contractile activity. Two weeks after abdominoperineal resection for carcinoma of rectum.

(e) Same patient. Typical slow contractions with potential pattern.

(f) Bona fide action potentials accompanying brief contraction of sigmoid colon succeeded by typical large movement artifacts as balloon was extruded through stoma. Colostomy two years old after abdominoperineal resection for carcinoma of rectum.

3-a and b). The implication is that the potentials do not originate as artifacts in variations of input resistance occasioned by electrode movements at the mucosal surface. By comparison such movement produces rather distinctive patterns (Fig. 3-f). The characteristic association of the potentials with intestinal contraction, moreover, would seem to rule out polarization artifacts as their source since the latter would hardly be expected to meet this limitation. In the later connection it is noted that bursts of potentials appearing independent of any detectable mechanical activity reproduce the patterns associated elsewhere with the onset of contraction (Fig. 3-d).

Potentials recorded from the intestinal wall under the above conditions cover a frequency spectrum from roughly 0.5 cycles per second to 15 cycles per second. Within this spectrum there is a definite tendency to exhibition of several rhythmic maxima. The characteristic prodromal electrical discharge, *e.g.*, is a brief rhythmic burst, usually at 9–12 per second (Fig. 3-a) although it may be as slow as 5–6 per second (Fig. 3-b) or as fast as 15 per second. The emergence of this burst precedes the onset of detectable mechanical activity by approximately 0.75–1.5 seconds. In its subsequent development the potential pattern evolves usually as a slow (0.5–1.0 cycles per second) random complex which fades out frequently at the peak of the intestinal contraction (Fig. 3-a). During sustained activity recurrent fast or intermediate rhythmic discharges are superimposed on these slow drifts often heralding new increments of contraction (Fig. 3-c). These general features of the potential patterns are in harmony with those reported by Forster, *et al.*[4]

Simultaneous tracings from two different areas of the intestinal wall exhibit moment-to-moment variations in relative predominance of discharge and changes in phase relations apparently reflecting a changing orientation of recurrent or prevailing electrical gradients with respect to the recording electrodes (Fig. 3-b and c).

The long latencies between electrical discharge and mechanical contraction are open to question and probably reflect in part both the lag and relative sensitivity of the motility recorder. In this connection, the significance of electrical discharges appearing in the absence of detectable recorded intestinal contraction is not clear (Fig. 3-d). These bursts reproduce the prodromal discharges associated with the onset of contraction. More sensitive means of recording motility might well reveal them as the precursors of luminal intestinal contractions. Their appearance without correlated mechanical activity would implement the logical theoretical allocation of their origin to the rhythmic beating of neurons in the myenteric plexus, already suggested by their clear-cut antecedence over muscular contraction and in harmony with the well-known rhythmic electrical properties of groups of nerve cells elsewhere (Berkson[6]). As such, these rhythmic potentials might well signal the discharge of efferent impulses to the mural smooth muscle the contraction of which, regulated by the impulses, is heralded by the emergence of the ensuing slower action potential complex.

SUMMARY

An apparatus for measuring intestinal motility and a technic for recording electrical action potentials of the intestinal wall in conjunction with motility are described, using an electrode-bearing modification of the Miller-Abbott tube. The action potential patterns are described in relation to contractile activity of the intestine and certain considerations relative to their validity are discussed with the conclusion that they represent bonafide electrical potentials originating in the mural tissues.

REFERENCES

1 Brody, D. A., Werle, J. M., Mescham, I., and Quigley, J. P.: Intralumen Pressures of the Digestive Tract, especially the Pyloric Region. A. J. Physiol., **130**, 791, 1940.

2 Abbott, W. O., Hartline, H. K., Hervey, J. P., Ingelfinger, F. J., Rawson, A. J., and Zetzel, L.: Intubation Studies of the Human Small Intestine. XXI. A Method for Measuring Intraluminal Pressures and its Application to the Digestive Tract. J. Clin. Investig., **22**, 225, 1943.

3 Ingelfinger, F. J., and Abbott, W. O.: Intubation Studies of the Human Small Intestine. XX. The Diagnostic Significance of Motor Disturbances. A. J. Dig. Dis., **7**, 468, 1940.

4 Forster, F. M., Helm, J. D., and Ingelfinger, F. J.: The Electrical Action Potentials of the Human Small Intestine. A. J. Physiol., **139**, 433, 1943.

5 Ingelfinger, F. J., and Moss, R. C.: The Motility of the Small Intestine in Sprue. J. Clin. Investig., **22**, 345, 1943.

6 Berkson, J.: Electromyographic Studies of the Gastrointestinal Tract. IV. An Inquiry into the Origin of the Potential Variations of Rhythmic Contraction in the Intestine: Evidence in Disfavor of Muscle Action Currents. A. J. Physiol., **104**, 67, 1932.

THE TREATMENT OF COMPOUND FRACTURES IN THE ITALIAN CAMPAIGN

BARBARA B. STIMSON, M.D.*†
NEW YORK, N. Y.

BECAUSE of the character of the Italian campaign, with its slow but steady advance, delayed occasionally by heavily defended positions, as at Cassino, but never forced to retreat, General Hospitals could be established relatively near to the forward areas and the definitive treatment of the patients undertaken without the fear of an unexpected urgent evacuation. Transportation was relatively rapid and patients were received at these Base Hospitals usually within a week after wounding, frequently within three days. The opportunity was, therefore, afforded to keep the patients under the observation of the same group of surgeons for a period unusually prolonged for war conditions. It is pertinent, therefore, to ask what lessons were learned from this experience which have a bearing on peace-time surgery.

Because this article is based on the personal experience of the writer who was with the British Army a few words of explanation are necessary. It must be remembered that the organization of the Royal Army Medical Corps is different from that of the Medical Corps of the Army of the United States. Details of the differences are not relevant to this article except in so far as they pertain to the matter in hand. During the Middle East and North African campaigns the Royal Army Medical Corps formed specialist teams composed of specially qualified medical officers with trained enlisted personnel and attached to strategically located General Hospitals. Patients requiring the care of such a team were routed to that hospital. This policy was continued during the Italian campaign. Chest teams, faciomaxillary teams, Orthopedic Centers, *etc.*, were placed where it was felt the best care of the wounded would be obtained. An Orthopedic Center consisted of two medical officers, one a Major and one a Major or Captain, two enlisted men acting as clerk and operating room orderly, four masseuses and one occupational therapist. It moved as a unit usually to an already established General Hospital. The writer was officer-in-charge of the 16th Orthopedic Center which was located at Pompeii, at Naples, and finally at Rome. The wounded were received at Pompeii from Anzio and Cassino usually within three or four days from the time of wounding. The initial surgery had already been done by the surgeons of the Casualty Clearing Stations and Field Surgical Units. The

* Assistant Professor of Clinical Orthopedic Surgery, College of Physicians and Surgeons, Columbia University, N. Y. Associate Attending Surgeon, Presbyterian Hospital and Vanderbilt Clinic, N. Y.

† Doctor Stimson was a Major in the British Army. She was one of the first women surgeons to hold such a post. Recently decorated by British Government for her work.

presenting problem was that of the reparative stage, delayed primary suture and definitive treatment of the fractures. This was also true in Rome, where casualties were sent from the Gothic Line attack.

The liaison between the Forward and the Base Surgeons was in many instances very close, for after a tour of duty at the front the Forward surgeons were posted back to a General Hospital and their places taken by Base surgeons. It will be a lasting regret of the writer that she did not get front line experience. It was through no fault of the authorities who had planned it but each time the opportunity presented, unforeseen circumstances arose to prevent her leaving her particular job.

Another difference between the Medical Corps of the two armies must be remembered, and that is the British shortage of medical personnel in comparison to the American. Closely allied to that fact in determining policies in the care of the wounded was the fact that the United Kingdom was a relatively small island rather heavily occupied by Great Britain and her Allies. Therefore, it was felt wiser not to rush the wounded home but to keep them until no harm could come to them through the inevitable delay in transportation until they reached their final destination. Especially after the Normandy landings, the hospitals in England were crowded to capacity and the doctors greatly overworked. Therefore, patients were retained under continuous supervision longer than was usual in the American forces.

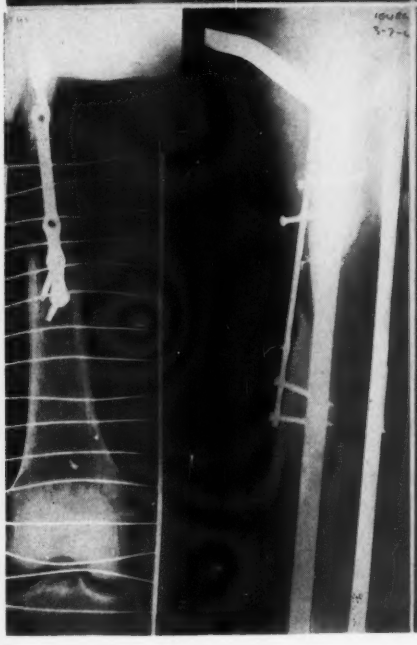
Patients with wounds or injuries involving the long bones and major joints and all complicated problems of fractures and dislocations were sent to an Orthopedic Center. It was neither possible nor necessary for such a Center, with its 200 beds, to cope with all fractures and one of the duties of the orthopedic specialist was to give advice on fracture problems in patients with abdominal, chest or head injuries on other wards. The coöperation and sharing of experiences between the various services not only within the hospital but also in the hospitals of the area was of the utmost value in clarifying and debunking impressions.

Because of this exchange of opinion and observation, not only between Forward and Base surgeons but also between surgeons of many nationalities but common interests, which the type of campaign allowed, certain principles in the treatment of compound fractures were emphasized anew, others were established.

The sooner compound fractures can be débrided the better. That is a well-recognized fact in civilian surgery. During the press of battle, however, with the casualties flooding the Casualty Clearing Stations and with the inevitable delay in finding the wounded, operations were frequently unavoidably performed 24 hours or more after wounding. Débridement had to be done with the removal of clothing, dirt, shell fragments and devitalized tissue. With careful surgery, adequate immobilization and with chemotherapy these patients reached the Base in most instances without spreading infection and in many instances with clean granulating wounds suitable for delayed closure. Some patients reached the Base Hospital with untouched wounds because

1-A

1-B



1-C

1-C (Cont'd)

FIG. 1.—(A) Shell wound of thigh, original roentgenograms.
(B) Lateral view.
(C) The same following overenthusiastic removal of fragments and ill-advised internal fixation.
(C Cont'd) The inevitable result two and one-half months later.

of multiple injuries and precarious general condition. For example, two weeks after wounding, pieces of battle dress and a part of a first field dressing which the patient had carried in his hip pocket were removed from the thigh of an officer who had sustained a severe head injury. The day after arrival these were débrided and left open; calcium penicillin sulfathiazole powder insufflated in the wound and penicillin administered systemically. In no case did a systemic infection result.

2-A 2-B 2-B (Cont'd)

FIG. 2.—(A) Shell wound of thigh, on arrival at the Base.
(B) The same 5 weeks later—wounds healed. Callus formation evident.
(B Cont'd) Lateral view.

However, these late débridements were uncommon. Working many times under heavy pressure the Forward surgeons somehow managed to débride meticulously as many as 14 wounds on one patient. Experience proved that the initial operation on compound fractures should strive to create a saucer-like wound, with transverse incisions of the fascia and longitudinal extension of the skin wound. Removal of all loose bone fragments was not only unnecessary but unwise as the fragments provided a needed source of calcium and if the wound became infected could be removed as sequestra later. With delayed suture the chance of infection was sufficiently lessened to permit the retention of loose fragments as a routine procedure (Figs. 1, 2 and 3).

Vaselined gauze was used as a wound dressing but was gradually discarded in favor of fine-mesh gauze which could not act as a plug and did not macerate the skin edges and make delayed suture more difficult. Following operation the extremity was immobilized usually in some plaster of paris encasement, a thoracobrachial for the upper extremity and a modification of the Tobuk splint for the lower.

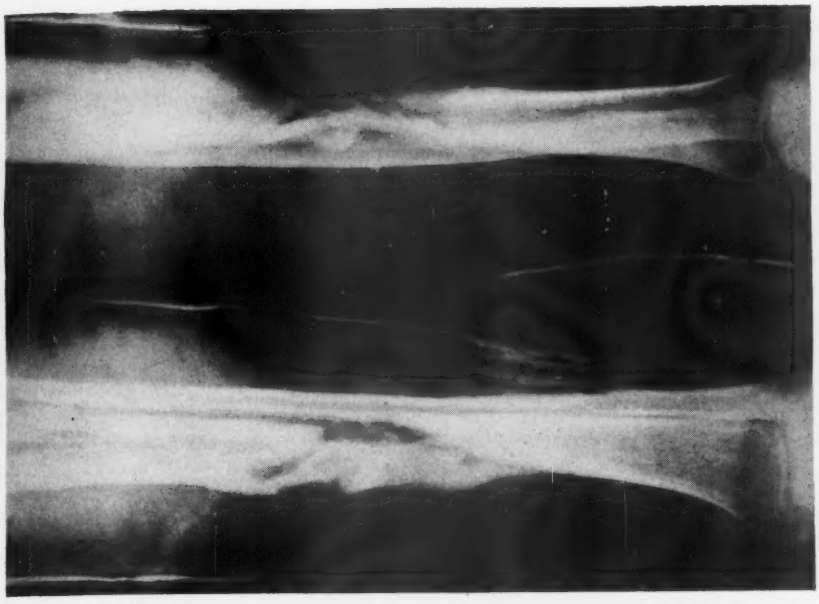


FIG. 3-B.—The same four weeks later. Fragments incorporated in callus.

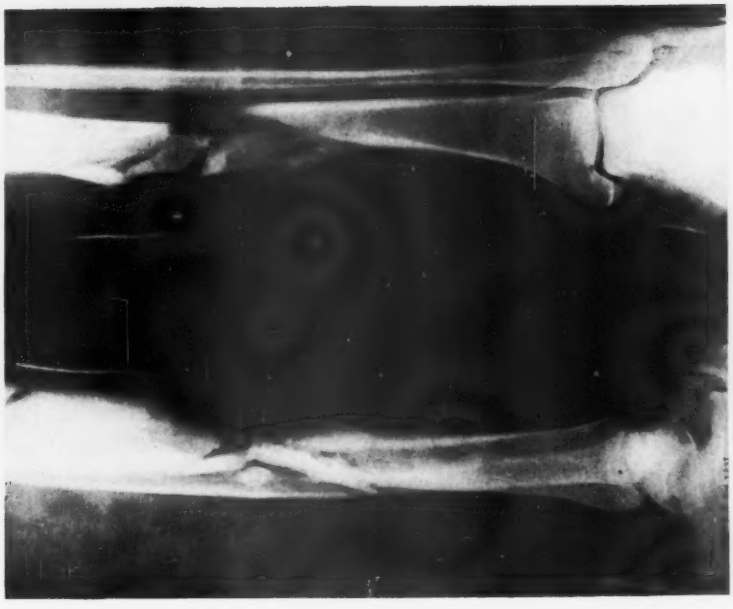


FIG. 3-A.—Shell wound of leg, on arrival at the Base.

Unless the condition of the patient or of the extremity indicated it immobilization and dressing were not disturbed until the patient reached the General Hospital. Intermediate and unnecessary dressings, just for a "look-see," increased the risk of secondary infection, and wounds which had been disturbed once or twice in transit did not look so well when they were dressed at the Base. Appearance had to be the criterion for there was no time for bacteriologic studies.

FIG. 4.—Compound fracture of both bones of the leg, on arrival at the Base three and one-half weeks after injury.

On arrival at the Orthopedic Center the wounded were quickly inspected and in most cases of multiple wounds and in all cases of compound fractures of the femur were given transfusions of whole blood. Hematocrit studies in these patients were uniformly low and their response to transfusions was spectacular. The day after arrival the wounded were taken to the operating room *via* the Roentgenologic Department and their wounds inspected. If the wound was covered with bright pink granulation tissue, the skin pinkish-white and elastic, a delayed closure was performed regardless of the existence of an underlying fracture. Meticulous hemostasis was essential with the careful removal of all blood clot. The skin edges could be mobilized by gentle, blunt dissection and surprisingly large areas could be covered. The most satis-

factory suture materials were dermol and silkworm gut, for it was found that thread became moist and gave less satisfactory scars. Inverted mattress stay-sutures under considerable tension, going from deep to superficial tissue and being placed near the ends of the wound first enabled the operator to close the skin edges with interrupted sutures in extremely large wounds. Complete closure was the aim, for those cases gave the highest percentage of satisfactory results. Drains were used only in rare instances. As has been said before the decision to close had to be made on the appearance of the wound on the operating table. There was no time to wait for bacteriologic reports.

Certain wounds, especially those of the buttock, were closed around fine-bore tubes to allow instillation of penicillin. This has been done even in the presence of obvious contamination and surface infection, because it was found that the skin protection, with the increased comfort to the patient, the diminution of tissue fluid loss and the protection from further contamination outweighed the danger of increased infection. Frequently the skin sutures would not hold and had to be removed at subsequent dressings but the wound was always markedly diminished in size. In some cases it amounted to a life-saving measure when coupled with the usual supportive and systemic measures.

Following the treatment of the wound the fracture problem was considered and definitive measures instituted, in some cases skeletal or skin traction, in others plaster of paris splints. Circular plaster encasements were avoided in compound fractures where possible because of the necessary inspection of the sutured wounds. Posterior molded and sugar-tongs splints were found to be time-saving and adequate for leg and ankle fractures. One or both limbs of the sugar-tongs could be pulled out to allow access to the wounds without disturbing the position of the bones.

It was found that earlier reposition of fractures might have been wise. Some patients were delayed in reaching the Base Hospitals and adequate reduction was made difficult, if not impossible. In some instances it was felt that the bone ends might have been slipped together at the time of the initial operation (Fig. 4).

Internal fixation of fractures caused by shell fragments is not feasible in most instances because of the gross comminution of the bone ends. The few cases that seemed to be suitable for plating were operated upon, as a rule, when the compound wound was healed, *i.e.*, the tenth day after suture. The operation was performed through a separate incision, the wound left open for five days and then sutured. It was found by experience that plating through the compounding wound was technically difficult and because the decision to use internal fixation could not be made until the patient was on the table and the wound inspected it was administratively difficult. It proved wiser to make it a planned procedure. Where the method was used it proved satisfactory, with no complications within the first three months.

All sutured compound wounds were dressed in the operating room at five-day intervals until healed. This method began as a matter of expedience because of the shortage of personnel but proved to have definitive advantages.

It was found that wounds that could not be closed completely at the first attempt could frequently be drawn together by a few additional sutures at five days. If not, grafts could then be placed. If there was any evidence of undue tension or of infection sutures could be removed. An anesthetist was always available so any necessary procedure could be undertaken painlessly and unhurriedly. Dressings were done at the end of the operating list, with operating room technic so that the risk of secondary infection was minimized.

Penicillin was not used routinely on all wounded by the British in the Italian campaign, especially in the early days when the supplies were limited. The sulfa drugs were used systemically but frequently in transit the doses were skipped or omitted entirely. The local application of calcium penicillin sulfathiazole powder was used in certain Forward areas and in many of the General Hospitals. In spite of the lack of uniformity in the use of chemotherapy, however, the wounds treated in accordance with surgical principles by experienced surgeons were amazingly clean and the results of delayed primary suture were satisfactory in a high percentage of cases. Sufficient credit can never be given to the excellence of the surgery in the Forward areas. It is undoubtedly true that penicillin gave the necessary impetus to the use of delayed closure in compound fractures caused by war wounds. Its psychologic value was great; its absolute value will emerge when all the data have been assembled and analyzed.

What, then, has been learned? Most of the lessons are not new—early, adequate débridement, immobilization, wound closure as complete as possible within ten days, infrequent dressings, general supportive treatment especially with blood. Even under war conditions the adaptation of the treatment to the needs of the individual must be maintained. Mass production methods should not be used except in periods of intense pressure. Operations, such as internal fixation (Fig. 1), should not be undertaken unless operating room facilities, adequate instruments and qualified surgeons are available. Under stress, when the snowball of work to be done keeps rolling up, standards tend to slip. They should, however, be kept constantly in mind and the effort made to keep them at their highest level.

The writer wishes to express her deep appreciation of the understanding, coöperation and encouragement of Major General Munro, Consulting Surgeon to the British Army; Brigadier W. Rowley Bristow, Orthopedic Consultant to the British Army; Brigadier Harold Edwards, Consulting Surgeon, and Lt. Col. Alan Watson, Orthopedic Advisor to the British Central Mediterranean Forces.

GUNSHOT WOUNDS OF THE ABDOMEN

FREDERIC W. TAYLOR, M.D.

INDIANAPOLIS, IND.

FROM THE DEPARTMENT OF SURGERY, INDIANAPOLIS CITY HOSPITAL, INDIANAPOLIS, IND.

IT WOULD SEEM that no useful purpose could be served by adding another discussion to the deluge of papers which have appeared recently on the subject of abdominal wounds. This seems particularly true since the present report deals primarily with such wounds in civilian experience rather than military service. There are, however, several important features in comparison with Service experience that should be emphasized.

A few years ago the writer reported the results of 101 consecutive gunshot wounds of the abdomen treated at the Indianapolis City Hospital.[1] This included the eight-year period 1930 to 1938. The changes that have been incorporated in general surgical care since that time are justification enough for continuing the study for another eight years into the era of plasma, sulfonamides, and penicillin. It should be recalled that late in the period 1930-1938 sulfonamides were just making their entrance into surgery, the general use of plasma was not to appear for several years, blood banks were unknown and blood was obtained from relatives who were often unwilling.

A continuing study such as this has the advantage that the type of patient, the institution, and the general capabilities of its personnel remain much the same; therefore, a change in medical care can be better evaluated than comparing the results in two dissimilar institutions or communities.

In the previous study (1930-1938) certain conclusions were drawn and recommendations made. These along with the pertinent findings of others in this pre-war period are as follows:

1. Our general mortality of 59.8 per cent for all cases operated upon for perforation of the abdominal cavity seemed excessively high. This, however, was quite in keeping with other large and unselected series. The general mortality throughout the country stood at a challenging 60 per cent. (McGowan,[2] 59.3 per cent; Oberhelman and LeCount,[3] 61.4 per cent; Prey and Foster,[4] 72.7 per cent.)

2. As might be expected, multiple visceral injuries caused a very definite increase in mortality. Thus, when both solid and hollow visceral injury occurred, 88.2 per cent of the patients died.

3. It was pointed out that well over half of our deaths occurred within the first postoperative 24 hours (58.5 per cent), and 45.3 per cent took place during the first 12 hours. But 28.3 per cent were considered to have died of peritonitis or its sequelae.

4. The conclusion seemed obvious that the majority of deaths following perforating gunshot wounds of the abdominal cavity were the result of shock —shock either from excessive blood loss, operative shock, or shock from extensive fecal contamination of the abdominal cavity.

5. The answer to this was intravenous blood in large amounts. How well this was carried out and with what result may be seen from the present report.

During the eight-year period from 1938 to 1946 there were 84 admissions to the Indianapolis City Hospital for gunshot wounds of the abdomen. This was a slight though not significant decrease over the 101 such admissions seen during the previous eight years. There seemed to be no lack of gun-play among the citizens on the home front although this was considerably less accurate than formerly noted. Of the 84 admissions, 15 were found not to have perforations of the abdominal cavity. These nonpenetrating cases need not enter into our discussion since, aside from some rather large retroperitoneal hemorrhages, they presented none of the problems of the perforated viscus. All survived.

There remained 69 cases of abdominal cavity perforation. Of these 25 died, a mortality of 36.2 per cent as compared with the mortality rate in the previous series of 52 per cent.

A further breakdown of the mortality is given in Table I. Here, it will be noted that the mortality was quite reasonable where a single viscus was

TABLE I

MORTALITY COMPARISON

	1930–1938		1938–1946	
	Cases	% Mortality	Cases	% Mortality
Patients having perforation of abdominal cavity	87	52	69	36.2
Perforation small intestine (including stomach)	11	45	8	0
Perforation colon (including rectum)	12	33	6	33
Perforation solid viscus (pancreas, liver, spleen, kidney)	10	70	19	5.3
Perforation both colon and small intestine	13	61	13	61
Perforation colon and /or small intestine and solid viscus	17	84	20	70

involved. Thus, there were no deaths in the eight cases in which the small intestine or stomach alone were perforated. It should not be construed that the anatomic damage was less severe, for such was not the case. Practically all these patients had multiple perforations and one as many as 12 perforations of the small bowel. However, it does mean that the lesion was localized to one given area and organ. This apparently makes for a much better prognosis even though some multiple visceral lesions seem less in extent and with less peritoneal contamination than those of the single viscus. It is also noted that the mortality for wounds involving both hollow and solid viscera was 70 per cent. An extremely high figure is common in all such cases reported.

The improvement from a general mortality of 52 per cent in 1930-1938 to 36.2 per cent for 1938-1946 is quite significant. To what may this be attributed?

First of all, the type of patient treated throughout both periods has remained the same. Four out of five were young adults who have been on the debit side of the municipal ledger all their lives and will continue so.

Fortunate it is for them that no one balances the books or that those to whom their care is delegated do not have to pass on their economic value to the community.

Second, the personnel and the institution have remained relatively constant. There has been a better understanding on the part of the doctors as to the physiologic factors involved in such cases, but the operative procedure has shown little variation.

Third, between the 1930-1938 series and the 1938-1946 series a revolutionary step has been made in the preoperative and postoperative care of the patient—the general use of plasma, sulfanilamide, and penicillin.

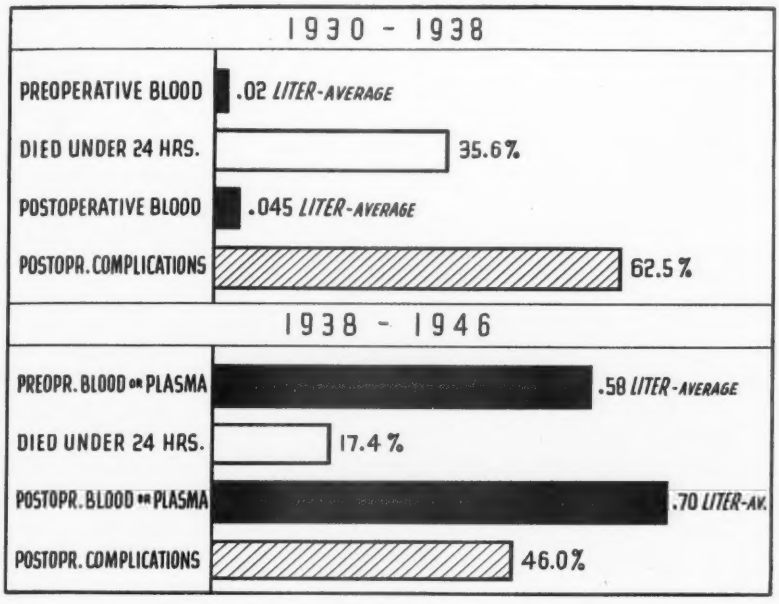


CHART I

PLASMA

Referring to Chart I it will be noted that a negligible amount of blood was given to the first series of patients in the form of transfusions. This all-important phase of therapy speaks for itself when it is noted that 35.6 per cent of these patients died during the first 24 hours after hospitalization. Such deaths can only be attributed to shock—shock from blood loss, extensive peritoneal contamination, or from the operative procedure. A sizable decrease in these 24-hour deaths is noted in 1938-1946 series (17.4 per cent). This improvement is attributed entirely to the increased use of blood and plasma. The amount used averaged .58 liters preoperatively and .7 liters postoperatively, and is small compared with the military use of three and four liters of plasma in similar instances. Undoubtedly some of our civil deaths were the result of insufficient blood or plasma.

SULFONAMIDES AND PENICILLIN

It has been the hope of everyone dealing with the contaminated peritoneum that the sulfonamides or penicillin would be the long-sought panacea. Such has not been the writer's experience. There is nothing in the present cases to suggest any alteration in the intra-abdominal infection brought about by these drugs. Penicillin or the sulfonamides were never life-savers so far as the peritoneal cavity was concerned. Mortality rates remained identical whether or not they were used.

There was, however, a definite though not too significant decrease in the complications following surgery (Table I). For this reason, and this reason only, penicillin or sulfonamides should be used routinely. Their use as a life-saving measure for the primary lesion only fogs the issue and the surgeon is too apt to put faith in the mystic drug rather than in surgical principles and treatment of potential shock.

In this connection, it might be well to mention the local use of sulfonamide. In the 1938-1946 series, sulfonamide powder was used locally in 13 instances. No benefit was noted. The powder was poured on some supposed critical area, dusted over the exposed intestines or smeared with the fecal contamination over uninvolved loops of bowel. Certainly, such practices are surgically unsound and at best are merely a means of temporarily raising the sulfonamide in the blood to an unpredictable level.[5, 11]

COMPARISON WITH SERVICE ABDOMINAL WOUNDS

From the standpoint of the actual lesion and the surgical problem, civil gunshot wounds and those in the Service are the same. There seems to be no significant difference in service mortality between small arms wounds and shell fragment wounds.[6,7] Likewise, there are few wounds from high explosives which are more mutilating than a shotgun charge at close range. There were ten such wounds in the last eight years, with five deaths.

The recent mortality records of Service wounds of the abdomen are considerably better than those seen in civil life. There are several obvious explanations for this fact. First of all, there has been insufficient time for the accumulation of any appreciable number of civil cases since the general use of plasma, penicillin, or sulfonamides. Practically all recent reports have been from the Services.

Second, there are a few Service cases who die before they are transported to the Forward Hospital. These deaths are, therefore, not included in any surgical analysis since they are not seen. On the other hand, all such cases are seen in the civil hospital and are included in the mortality analysis. In the field the lag-time between wounding and hospitalization is quite variable. In the survey by Imes[7] it averaged 11 hours. Ogilvie[8] reported that less than half of their cases were operated upon under 12 hours after injury. In the Indianapolis City Hospital cases the interval of injury to hospital averaged .7 of an hour. More than 20 per cent of the deaths occurred during the first 12 hours following injury. Admittedly, the treatment given during this time-inter-

val may not have been ideal from the standpoint of antishock therapy but nevertheless most of these patients would not be included in any military survey. They would have died before reaching the operating unit.

Third, no single Service hospital can follow all their cases to convalescence. A small number die or are lost to follow-up after evacuation from the unit originally reporting operative results.[7,8]

A few of the Service mortality rates which have been reported for penetrating wounds of the abdomen are as follows: Ogilvie, 43.4 per cent; Jarvis, *et al.*, 28.7 per cent; Bradford, *et al.*, 25.5 per cent; Imes, 20 per cent. A review by Sloan on 35 civil cases treated recently reports a mortality of 14.3 per cent.

There is no essential difference in the surgical treatment of civil or military abdominal gunshot wounds. It is a little disappointing that no improved routine has sprung from the large numbers of Service cases which have been reviewed. Plasma was always handy in large quantities and was used in ever increasing amounts. The same cannot be said of the civil institutions where plasma was often not too plentiful. The Service dictum to "exteriorize all wounds of the colon" was greatly overemphasized. There is no reason to exteriorize the simple puncture wound of the large bowel. It can be closed perfectly safely and is followed with a convalescence which is far more satisfactory to the patient. Of course, large rents, devitalization, and retroperitoneal wounds of the colon demand exteriorization.

It would be of interest to know what part overlooked perforations of the gastro-intestinal tract played in the mortality of Service cases. No such figures have been reported. If this incidence approaches that of civil cases, it may be estimated that one-third of the Service deaths were associated with lesions overlooked at the operating table. It is obvious that there will always be overlooked perforations since at times the condition of the patient may not warrant methodical search of all viscera. However, with the increasing use of plasma and control of the patient's shocked state, there should be ample opportunity for a more thorough search and less hurried repair.

With the further realization of the importance of the patient's shock, or his potential shock, as the dominant feature in the care of these cases, it is expected that the general mortality for gunshot wounds of the abdomen will decrease considerably in civil institutions. There will always be a sizable mortality in this type of injury. The resultant mortality will be in direct proportion to the extent of intra-abdominal injury. The cases here reported run quite parallel in this respect to those of Imes, who noted that the type of missile, time-lag before operation, principal viscus involved, and extent of peritoneal contamination were of secondary importance.

SUMMARY

1. A comparison is drawn between gunshot wounds of the abdominal cavity treated at the Indianapolis City Hospital during the period 1930-1938 and during the subsequent eight years, 1938-1946.

2. The mortality during the recent series was 36.2 per cent as compared with 52 per cent in the former.

3. This improvement is attributed entirely to the realization that shock or potential shock is the principal factor to be considered in treatment. Plasma became available during the second period and was used as much as a somewhat limited supply would permit.

4. The sulfonamides and penicillin also came into general use during the second eight-year period. So far as could be determined, these drugs did not alter the course of the intra-abdominal lesion. Likewise, they did not alter the mortality.

5. The use of a sulfonamide or penicillin is advocated in all these cases but not because of what the drugs can do to the intra-abdominal lesion and its subsequent peritonitis. They are advocated for their ability to decrease the complications following operation. When an operator becomes too conscious of the virtues of sulfonamide or penicillin he tends to lose sight of surgical principles. It would be far better to realize that at the present time nearly half of these patients who are going to die, die presumably of shock during the first 24 hours. After that time a few more will die from overlooked bowel perforations.

6. Military and civil mortality statistics cannot be directly compared because military cases are to some extent selected. Medical care has been essentially the same in both groups.

REFERENCES

1 Taylor, F. W.: Gunshot Wounds of the Abdomen. J. Indiana State M. A., **31**, 342, June, 1938.

2 McGowan, F. J.: Penetrating Wounds of the Abdomen. ANNALS OF SURGERY, **102**, 395, September, 1935.

3 Oberhelman, H. A., and LeCount, E. R.: Peace-time Bullet Wounds of the Abdomen. Arch. of Surg., **32**, 373, March, 1936.

4 Prey, D., and Foster, J. M.: Gunshot Wounds of the Abdomen. ANNALS OF SURGERY, **99**, 265, February, 1934.

5 Taylor, F. W.: Misuse of Sulfonamide Compounds. J. A. M. A., **118**, 959, March 21, 1942.

6 Jarvis, F. J., Byers, W. L., and Platt, E. V.: Experience in the Management of the Abdominal Wounds of Warfare. Surg., Gynec. and Obst., **82**, 174, February, 1946.

7 Imes, P. R.: War Surgery of the Abdomen. Surg., Gynec. and Obst., **81**, 608, December, 1945.

8 Ogilvie, W. H.: Abdominal Wounds in the Western Desert. Surg., Gynec. and Obst., **78**, 225, March, 1944.

9 Bradford, B., Battle, L. H., and Pasachoff, S. S.: Abdominal Surgery in an Evacuation Hospital. ANNALS OF SURGERY, **123**, 32, January, 1946.

10 Sloan, H. E.: Perforating Abdominal Injuries. Surg., Gynec. and Obst., **79**, 337, October, 1944.

11 Wilkinson, R. S., Hill, L. M., and Wright, L. T.: Gunshot Wounds of the Abdomen, Surgery, **19**, 415, March, 1946.

SKIN-GRAFTING THE BURNED DORSUM OF THE HAND

GEORGE V. WEBSTER, M.D.
PASADENA, CALIF.
AND
LIEUT. WILLARD D. ROWLAND, M.C., U.S.N.R.
NATIONAL NAVAL MEDICAL CENTER
BETHESDA, MD.

THE PHYLOGENETIC DEVELOPMENT of the hand of Man has led to specialized adaptation of its skin covering. The skin of the volar surface is thickened, horny, and is capable of withstanding considerable mechanical friction, replacing the epidermal cells lost in such function by a continuous proliferation of new keratinized layers. In addition, the trabeculated subcutaneous fat pad is designed to protect the hand from mechanical shock occurring when moving objects are caught in the palm of the hand, or rough objects are handled. The palmar skin is also capable of contraction, and of folding upon itself in well-outlined patterns of skin lines, to accommodate itself to the decrease in volar surface area with each clenching of the fist. The skin of the dorsum is complementary in function to the palmar skin. It is not subject to excessive friction nor mechanical shock except when the closed fist is used for striking an object or an opponent in fighting. It is, therefore, relatively much thinner than the volar skin and is provided with little or no subcutaneous fat pad. Its resistance to trauma is poor and the skin is quite different in character from the palm. The major feature of the dorsal skin, however, is its high degree of elasticity. This is necessary to accommodate itself to the large increase in surface area when the fist is clenched. It must retract again quickly when the fingers are outstretched and, thus, it exactly counterbalances the contraction and folding of the palm in flexion and the extension of the fingers in extension.

In burns of the dorsum of the hand, the above conceptions of normal structure are necessary to fully understand the burn problem. Since the skin is thin, its elastic fibers are near the surface and are, thus, easily damaged by thermal injury which would not be as harmful on another part of the body. Also, although a second-degree burn may be completely healed without grafting, there may be sufficient damage to these important structures, so that hand function is definitely impaired. In third-degree burns, of course, the elements of local bacterial invasion, with subsequent fibrosis and stiffening, seriously cripple the normal function in this highly specialized area.

Flexion of the fist is a dominant action over extension. This is noted in the increased power of the flexors over the extensors and in the grasping

* The opinions or assertions of the Junior Author are the private ones of the writer and are not to be construed as official or as reflecting the views of the Navy Department or the Naval Service at large.

FIG. 1

reflex. In addition, protective reflexes, such as covering the face with the hands, result in protection of the palmar surface and exposure of the dorsum. These two factors are undoubtedly responsible for the vast excess in incidence of burns of the dorsum over burns of the palm of the hand. It is, thus, true that in any large number of burns, such as have been encountered during World War II, burns of the dorsum of the hand are exceedingly common. Their consideration as a separate surgical problem is, therefore, desirable.

CLASSIFICATION

The familiar classification of burns into three "degrees" should be further subdivided when discussing burns of the dorsum of the hand, as each subdivision presents its own special problems of treatment. First-degree burns are subdivided into two groups, second-degree into three groups and third-degree into three groups (Table I). Such a subclassification is helpful in visualizing the progressive stages of injury to the hand by the burn, and will possibly be of some aid in selecting methods of treatment, and in giving an ultimate prognosis. The classification is accompanied by a tabulation of the depth of injury, together with the clinical appearance in relation to the time interval following injury. In a separate column are listed the types of skin-grafts indicated at both early and late stages in the care of the burned hand. These subdivisions are, of course, only rough approximations, but they may serve to guide the surgeon in the conception of the use of the "temporary" graft which is emphasized later in this paper.

EARLY CARE OF THE BURNED HAND

Scores of writers have emphasized the value of early grafting of burns. In brief, the advantages of such early grafting are those of rapid closure of the open wound produced by the burn. In so doing, the loss of body fluids is stopped and the contaminated, open wound is rendered sterile soon after

---

FIG. 1.—(A) Right hand and wrist of a four and one-half-year-old girl who caught her hand in a mangle where it burned for 15 minutes because of failure of the release mechanism. The burn was so deep, and the child's condition was so poor that amputation had been considered by some doctors who saw her. Appearance of the hand when first seen, three weeks after injury.

(B) Granulating wound after active local treatment of the burned area by frequently changed wet dressings of normal saline solution and daily saline baths. All extensor tendons as well as the dorsum of several bones have been destroyed. The metacarpophalangeal joints were completely open and the cartilage sequestrated.

(C) Appearance after use of small deep grafts as "temporary" covering for the raw surface. Bits of bone are still sequestrating, but the wound is nearly healed and the patient is out of the hospital.

(D) Resection of all scar and "temporary" grafts and replacement with the permanent graft, a pedicle flap from the abdomen. The hand and wrist were fixed to the abdomen for 18 days.

(E) Nine months after the burn. The extensor carpi radialis tendon has been reconstructed, utilizing a scar-tissue band. Motion at the wrist is complete. The metacarpophalangeal joints will require arthroplasty at a later date, which, if successful, will be followed by grafts to the extensor tendons of the fingers.

healing has taken place. In burns of the dorsum of the hand, the need for early grafting is even more important than elsewhere on the body, for in few other areas is the fibrosis, which accompanies the prolonged healing of an open wound, so crippling in its late effects.

The above conception of the burn as a wound is important, for there is apt to be confusion as to the surgical care of this type of injury, especially because of the extensive literature on burn care, which somehow carries with it the idea that burns should be treated differently from other wounds. The major difference between burns and other types of wounds is that of surface area of the injury. As such, the problems of fluid loss and resultant changes in body physiology are tremendous, but they do not alter the fundamental conception of the local area of the burn as a wound which involves all of the elements of normal wound-healing physiology. All treatment is, therefore, directed toward closing of the wound at the earliest possible moment.

Methods of care of the local area of the burn will vary from surgeon to surgeon, but the fundamental surgical principles of cleanliness, compression and rest in the treatment of burns, as emphasized by Koch, have met with universal approval. One point should be stressed, however, in relation to the principle of rest. While it is felt that rest is of great value during the first few days of the burned patient's convalescence, the enormous experience of World War II has shown that if hands are splinted for more than a few days, however good the local healing, the stiffening and crippling of the metacarpophalangeal and finger joints far outweighs in importance any advantage to the healing wound surface. Prolonged splinting is definitely contraindicated. In fact, the hands which have done best have been those which have been exercised daily in baths of normal saline, keeping the joints elastic and the fingers movable. Thus, as soon as the body has had time to "wall-off" the damaged area by its normal protective mechanisms, which is ordinarily considered to be from a week to ten days, the exercises are begun. The patient himself finds encouragement as he begins to use his hands again after the fear of stiff and useless members has been established from the time of the burn. Such hands are mobile and flexible, and, after being subjected to the necessary immobilization for a few days at the time of grafting, they quickly regain motion during the postoperative period.

The general care of the patient is all-important and should be governed by the well-established rules for the treatment of burned patients. Nutrition, which is the fundamental basis of all wound healing, may become a special problem in the patient with both hands burned, for he is unable to feed himself from the time of injury. Unless special care is taken to see that he is adequately fed, his qualitative and quantitative food intake may fall far below his requirements. Food needs of the burned patient are greatly in excess of the normal food intake required in everyday life, because of the mass of tissue replacement which is necessary and the constant loss of protein and metabolites through the wound. It is, therefore, desirable that at least four and sometimes six meals per day be given, stressing a high-caloric and high-

protein intake. If the patient's appetite is not good enough to tolerate this forced feeding, supplementary feedings can be given by stomach tube and parenteral therapy of plasma, whole blood and intravenous glucose and amino-acids. The use of amino-acids intravenously is costly and, at best, is a poor substitute for autosynthesis from protein foods taken by mouth, and, thus, has not been extensively used in our experience. The vitamin intake should be kept up in the food and supplemented by additional oral therapy when necessary. The beneficial effects of high-vitamin intake on wound healing have been well shown.

Chemotherapy is given intensively during the first few days of the burn while the body is organizing its defenses against the massive bacterial invasion. Sulfadiazine is the drug of choice by mouth, and penicillin is given parenterally. The use of chemotherapy is then stopped and its help is reserved for acute episodes of infection and for preoperative and postoperative medication at the time of skin-grafting.

"TEMPORARY" SKIN-GRAFTING

After preparation of the wound for grafting, the surgeon is faced with a choice of grafting methods. It is here that the principle of "temporary" grafting is of importance. By "temporary" graft, we mean the application of skin-grafts, the sole purpose of which is to close the wound. Such grafts are usually removed and replaced with good skin at a later date when the conditions under which the surgery is performed are much more satisfactory. The temporary graft has for its object the most rapid epithelization of the wound and the conservation of donor skin. The grafts used may be "stamp" grafts, cut from a dermatome sheet; "patch" grafts, cut from a free-hand, thick-split graft, which can be easily cut into bits or patches of skin; or "small deep grafts," as described by Davis. Small islands of skin of this type can quickly cover a large granulating area on the dorsum of the hand and forearm with scar epithelium, with a minimum destruction of good donor sites. The chief objection to the use of "small deep grafts" has been their destruction of good skin which may be needed for late repair. For this reason, the "stamp" or "patch" grafts are nearly always preferred. There is one advantage in the "small deep grafts," however, which is the introduction of the elastic elements of the deeper layers of the skin. In addition, their resistance to infection in the granulating area is somewhat higher than the other types, and for this reason, their use is sometimes justifiable. If they are taken from the "swimming-trunk area," a few grafts of this type can often be obtained from a region which is unsuited to split-graft technics, and as it is always hidden by clothing, except in the nude, it thus eliminates disfigurement (Fig. 1).

It is occasionally possible to place the "permanent" graft directly on the granulating surface and secure an excellent end-result at a single operation. This procedure has been advocated for many years by a number of plastic surgeons, and when cases are properly selected, choosing a patient in excel-

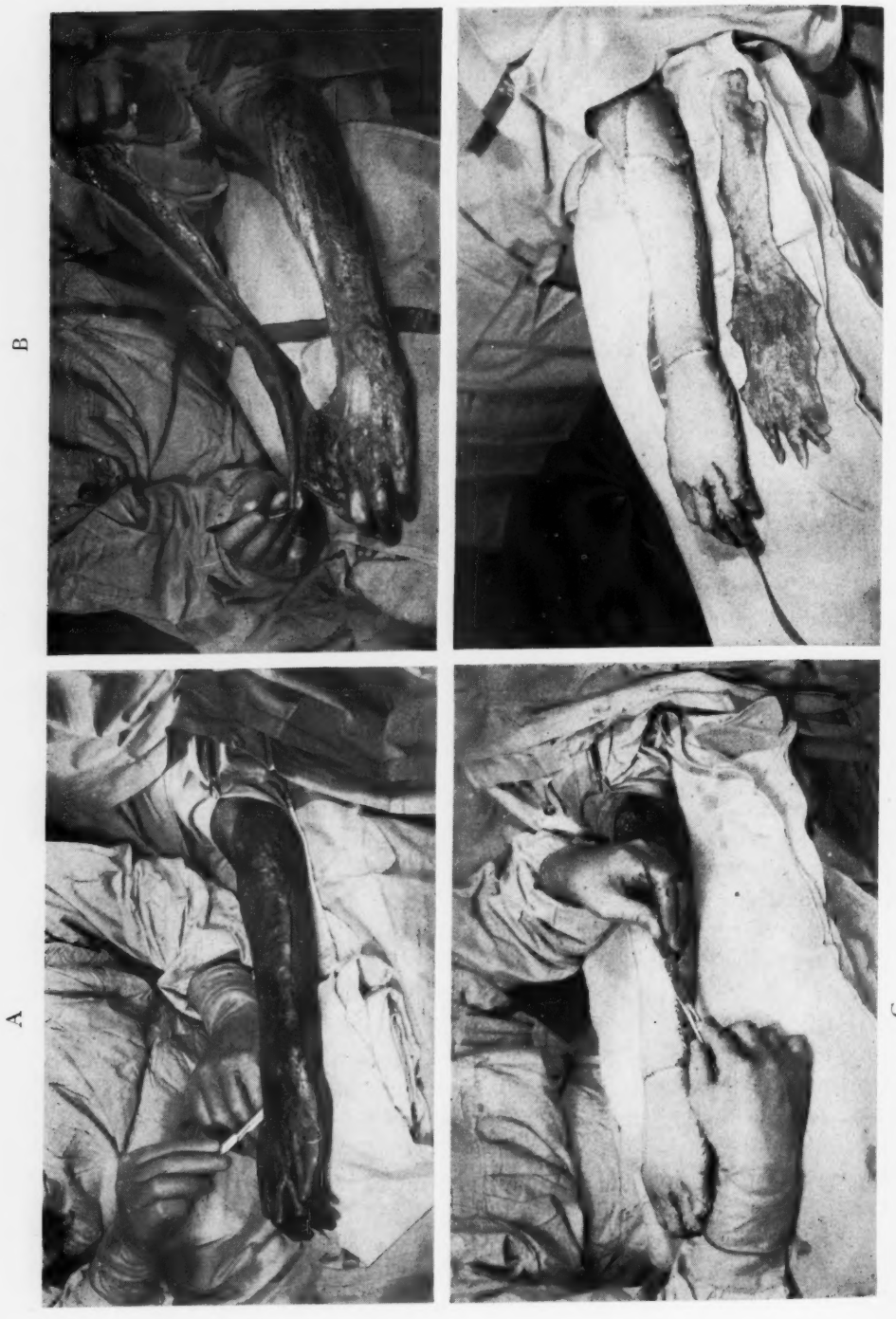


FIG. 2

lent condition, with a uniform depth of burn, the single stage application of thick-split skin grafts is certainly the method of choice. All too often, however, the result of such primary use of the large sheets of graft are disappointing. The marginal scar becomes hypertrophic, contracture of the scar-tissue bed causes wrinkling of the graft, webbing occurs between the fingers and secondary operations are then required to obtain a satisfactory result. It would seem obvious then, that the maximum conservation of skin and the best cosmetic and functional result can be obtained by the application of "temporary" grafts for rapid wound-healing, and then late radical resection of all scar tissue and replacement with pliable, elastic skin at a second operation (Figs. 2 and 3). The same working rule applies to second-degree burns which heal without grafting.

One objection has been raised to this two-stage method of repair, and that is the production of contractures as a result of the first operation. These contractures do occur (Fig. 1) but are completely relieved at the second stage of the operation. If the second stage is performed within a few weeks or months, the disability produced by such an interim contracture is negligible.

LATE SKIN-GRAFTING

There are numerous points which contribute to the good results of skin-grafting the burned dorsum of the hand at a time when the initial burn is healed and the patient is essentially a well individual. In the first place, the procedure is an elective operation. As a result, nutrition can be raised to a high level and the risk of respiratory and other complications can be reduced to a minimum. Second, the operative field is covered by intact epithelium, and if a little time has been allowed for blanching of the scars, the tissues are sterile, with little or no chance of residual bacterial activity in the scar. The advantages of such complete sterility of the wound are very great when compared with the open granulation tissue of the original burn, which is filled with an actively virulent bacterial flora of potential danger at all times. The hand can be incised freely at the late stage, removing all extensions of the scar without the danger of producing a spreading infection which may wreck the delicate mechanisms of the hand. Third, all scar can be removed at the late operation, and the graft is applied on normal underlying tissues. If the graft has been applied directly to granulation tissue or to the yellow base of connective tissue beneath the granulations, there is residual scarring beneath the graft which is inevitable. This scar is inelastic and always restricts the motion of the wrist and fingers to a certain degree. When the graft is applied

FIG. 2.—(A) Left hand and forearm encased in unyielding, hypertrophic dorsal scar and exhibiting many "patch" and "small deep grafts" applied elsewhere. At time of entry, six months after the burn, redness had faded from the scars to a considerable degree, and the danger of latent infection in the tissues was minimal.
(B) All scar and "temporary" grafts removed in one segment.
(C) Dermatome grafts being sutured in place, approximating edge-to-edge.
(D) The permanent skin-grafts in place, with the resected scar placed alongside the forearm for comparison of length.

to normal, sterile subcutaneous tissue, the amount of connective tissue beneath the graft is minimal. Fourth, the margins of the graft can be sutured to good skin under sterile conditions and the tendency for hypertrophic marginal scar is greatly reduced.

FIG. 3.—(A) Preoperative appearance of a deep second-degree burn which healed spontaneously, but exhibited marked hypertrophic scar formation and restriction of movement.

(B) Postoperative appearance after total resection of the dorsal scar on the right hand and partial resection of the dorsal scar on the left. Dermatome skin-grafts of even thickness produce this flexible, normal appearance and function.

FIG. 4.—Drawing of hand and wrist illustrating principles which have been found useful in planning incisions for resection of scar-tissue and "temporary" skin-grafts at the late stage of reconstructive surgery.

The technic of late skin-grafting of the burned dorsum of the hand follows closely the technic of all other operations on the hand. The hand and arm are carefully prepared the night before operation, paying particular attention

to cleaning and trimming the fingernails, which are often distorted in burn patients and have many pockets and crevices which retain dirt and bacteria. A 20-minute period of soaking in warm soapy water is followed by vigorous scrubbing by the patient himself for ten minutes. The hand and arm are then shaved and scrubbed with soap and water.

At the operating table, the patient is usually given a general anesthesia if the dissection is to be extensive, but local infiltration with one per cent procaine hydrochloride with adrenalin can be used for smaller scar resections. A blood-pressure cuff tourniquet about the upper arm is always used, and gives an excellent bloodless field for dissection if the arm is elevated for several minutes or is wound bloodless with an Esmarch bandage before the tourniquet is inflated. The amount of skin to be needed is estimated before operation and this skin is removed with the dermatome before dissection of the hand is begun.

The dissection of the dorsal scar is started by outlining the scar with an incision about its entire circumference. This outline will be the margin of the future graft, and must be carefully planned, so that the resulting scar will not cross a flexion crease at the wrist or finger-joints at right angles, producing scar contractures (Fig. 4). This is avoided by breaking the longitudinal lines with dart-like extensions at each flexion crease, as described by Brown and McDowell. Bunnell states: "In placing any type of skin graft, care should be used to avoid the median longitudinal line of juncture between the border of the graft and the skin, as this will lead to contracture and keloid. Where such a place seems unavoidable, one can make a cross-cut through the skin border and lay a projecting point of the graft in the gap. The degree of zig-zag thus furnished will help in preventing scar contracture."

Special attention should be given to division of the webs of the fingers to avoid recurring web-formation when the grafts have contracted and their marginal scar has been formed. It has been our practice to overcorrect this web division, splitting well down the volar aspect of the palm, almost halfway from the distal margin of the web to the distal flexion crease of the palm. The dorsal graft is then advanced to this extended point on the volar surface, providing good skin covering deep in the web, and leaving no potential web of marginal scar. Where sufficient care has not been exercised in this reconstruction of the webs, secondary operations for their correction have become necessary. One word of caution should be given in regard to this splitting of the volar skin pad to deepen the webs. The digital nerves lie just beneath the skin, and unless one is working in a bloodless field, they can be severed easily producing anesthesia of the affected finger.

After making the marginal incision completely around the scar, the entire scar-tissue mass is resected, carrying the dissection to the elbow or above, if necessary, to secure complete relaxation (Fig. 2). The dorsal branches of the ulnar and radial nerves lie in the field of dissection and should be preserved unless they were destroyed by the original burn. If they have been partially destroyed, sensation will often return to a more or less satisfactory

degree by overlapping from the volar branches and by some degree of arborization and regeneration of the injured nerves themselves.

After removal of all scar tissue, the tourniquet is released, and all major bleeding points clamped with mosquito hemostats and tied with fine silk or cotton. The arm is then elevated for a few minutes and the tourniquet is reinflated for the remainder of the operation. The graft is sutured in place, securing edge-to-edge approximation where possible, and pressure dressings and splints are applied before the tourniquet is released. The finger tips are left exposed from the dressing so that circulation can be checked.

Where the burn has been deeper and tendons or bones have been destroyed, the thick-split graft is not adequate and a pedicle flap of skin and fat must be applied. For this purpose, the direct one-stage flap from the abdomen is the simplest and best, necessitating a fixation period of 18 to 21 days (Fig. 1). New tendons can be grafted beneath such pedicle flaps and the joints of the wrist and metacarpophalangeal areas are supplied with adequate nourishment and mobile soft tissues which give the maximum chance for recovery of function following the burn injury. The application of pedicle flaps distal to the metacarpophalangeal joints is practiced in a few clinics, but the bulk of the flap produces an unsightly and unwieldy finger, regardless of the amount of "thinning" of the flap which is carried out. Grafting extensor tendons to the fingers beneath such flaps on the fingers has been accomplished by a few specially skilled surgeons, but the end-results of such surgery are, in general, very poor.

When all scar contracture has been released in the skin of the dorsum of the hand, there may yet remain contractures of the periarticular ligaments and connective tissue, which greatly limit motion. This is particularly apt to be true when the hand has been splinted on a flat splint with the fingers in extension at the time of the original burn. In this position, the ligaments are relaxed and rapidly contract into tight, firm fibrous bands which lock the fingers in extension. Restoration of motion in such hands requires the application of splints with traction loops about the fingers (Fig. 5). It is useless to try to stretch scar by such splints, and so they are applied only after all scar has been resected and the contracture released as far as possible by skin-grafting. At the time of surgery, capsulotomy is also performed, as recommended by Bunnell. If the extensor tendons are lightly adherent to the underlying bone, traction splints should overcome them. If the adhesions are more dense, complete tenoplasty may be necessary.

The splints employ the principle of fixed traction rather than elastic traction. The tension is increased on the finger loops by thumb-screw tension rods. The tension should be increased gradually over a period of weeks, and not made so tight as to cause redness and pain about the joints. This reaction will eventually increase the amount of local fibrosis and defeat the purpose of the splint. Elastic traction irritates the joints by constant minute motions under tension, and local tissue reaction occurs, with subsequent fibrosis. The splints are removed daily for active exercise periods and are then replaced and

adjusted by the patient himself. Massage and passive motion are strictly avoided, for they, too, increase the irritation of the periarticular tissues and the end-results are poor.

UNSOLVED PROBLEMS

There are a number of pathologic changes which occur as a result of burns of the dorsum of the hand which are difficult or impossible of correction by any known means at this time. One of these residual deformities is the distortion and destruction of the fingernails. The nail bed is warped and twisted

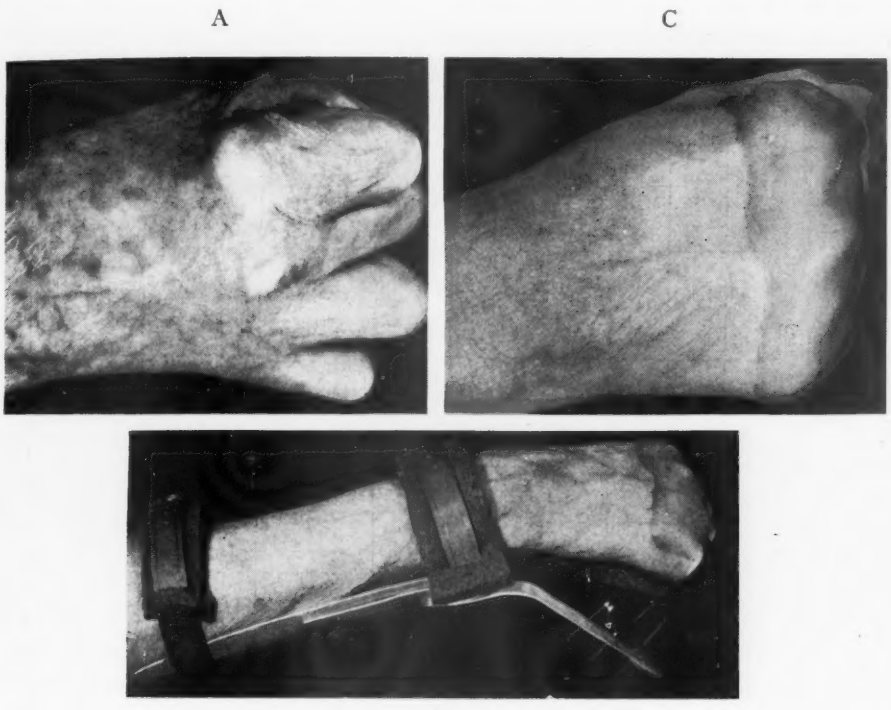


FIG. 5.—(A) Healed second-degree burn with marked restriction of motion at the metacarpophalangeal joints. The extensor tendons were intact.
(B) Splint used in obtaining further flexion of the metacarpophalangeal joints. At operation, capsulotomies were performed on these joints and skin-graft placed over the knuckles where the scar-tissue had become cracked and irritated.
(C) End-result, showing complete restoration of function. The pigmentation of this skin-graft makes it a poor color match for the surrounding skin, in spite of its excellent function.

so that the nail itself becomes a jagged, irregular horn. Removal of the nail gives but temporary relief until the nail grows back again. Its shape is not altered by the removal. To completely destroy the nail bed is difficult, and since there is no subcutaneous tissue to protect it from the underlying phalanx, the healed wound produced by excision of the nail bed becomes painful whether covered with a graft or allowed to heal by scar. Artificial nails have been

TABLE I

CLASSIFICATION AND GRAFTING METHODS FOR BURNS OF THE DORSUM OF THE HAND

BURNS OF THE DORSUM OF THE HAND
Classification and Grafting Methods

DEGREE OF BURN		DEPTH OF INJURY					CLINICAL APPEARANCE (If allowed to heal spontaneously, without graft)						TYPE OF SKIN-GRAFT INDICATED	
General Class	Sub-Class	Dermis, above epithelial islands	Dermis, down to the epithelial islands	Subcutaneous and areolar tissue	Tendons	Bones and Joints	Immediate	1 Week	2 Weeks	3 Weeks	4 Weeks	3–6 Months	Early	Late
FIRST DEGREE	A	Slight	None	None	None	None	Marked erythema.	Healed slight redness.	Healed normal appearance.	Healed normal appearance.	Healed normal appearance.	No contracture.	None	None
	B	Moderate	None	None	None	None	Erythema and moderate bleb formation.	Red desquamating.	Slight redness nearly normal appearance.	Healed normal appearance.	Healed normal appearance.	No contracture.	None	None
SECOND DEGREE	A	Severe	None	None	None	None	Marked bleb formation redness.	Remnants of bleb desquamating. Dermis red and tender.	Redness Desquamation.	Healed still red.	Healed pale to normal appearance.	Normal appearance. No contracture.	None	None
	B	Severe	Moderate	Slight	Slight	Slight	Some whiteness of dermis. Surface wet with body fluids.	White, wet. Surface becoming loose.	Whitish-Green, Dead layers separating. Few granulations forming.	Dead layers of dermis fairly dry, separating. Pink, healing dermis beneath.	Healed. Red. Slight tightness when making fist.	Nearly normal appearance. Some slight contracture may occur.	None	Rarely small area of thick-split skin-graft over knuckles may be needed.
	C	Total	Severe	Moderate	Slight	Slight	Dead white dermis. Surface wet with body fluids.	White, wet. Surface becoming loose.	Whitish-Green, Dead layers separating. Much exudate granulation tissue forming.	Most dead tissue separated. All surfaces granulating. Few epithelial islands visible.	Nearly healed by coalescence of epithelial islands.	Much contracture Severely scarred.	"Temporary" Graft At about Third Week a. Thin Thiersch graft b. "Patch" or "Stamp" grafts c. Small deep grafts	Total excision of all scar and replacement with thick-split skin-graft, preferably dermatome graft.
THIRD DEGREE	A	Total	Total	Severe	Moderate	Moderate	Dead white or blackened dermis. Surface wet with body fluids.	White, wet. Surface becoming loose.	Whitish-Green, Dead layers separating. Much exudate granulation tissue forming.	Most dead tissue separated. All surface granulating. No epithelial islands visible.	Granulating surface.	If healed, severe contracture.	"Temporary" Graft At about Third Week a. Thin Thiersch graft b. "Patch" or "Stamp" grafts c. Small deep grafts	Total excision of all scar and replacement with thick-split skin-graft, preferably dermatome graft.
	B	Total	Total	Total	Severe	Severe	Dead white or blackened dermis. Surface wet with body fluids.	White, wet. Surface, becoming loose.	Whitish-Green, Dead layers separating. Much exudate granulation tissue forming. Tendons or bones and joints exposed.	Much dead tissue. separated, Tendons and bones and joints exposed.	Granulating surface with tendons or bones and joints exposed.	If healed, severe contracture, useless joints and dense cicatrix, cracking and ulcerating.	"Temporary" Graft At about Fourth Week a. Thin Thiersch graft b. "Patch" or "Stamp" grafts c. Small deep grafts	Total excision of all scar and replacement with direct abdominal pedicle flap.
	C	Total	Total	Total	Total	Severe to Total	Charred hand, fingers partially destroyed.	Same, much discharge, beginning demarcation of dead tissue.	Dead tissue beginning to separate.	Active separation of dead tissue.	Active separation of dead tissue.	Unhealed, useless ulcerating stump of a hand.	"Temporary" Graft as soon as any granulating areas are clean enough to receive them.	Pedicle flap designed to give best functional reconstruction for the individual case.

tried without success, for the underlying bed is too irregular and the nails are a nuisance if the hands are used in any kind of work.

A second unsolved problem is that of loss of the extensor tendon on the dorsum of the finger. As has already been mentioned, the use of pedicle flaps in this region is undesirable, except occasionally for the index finger. The complete covering of all the fingers with a pedicle flap and then grafting new extensor tendons beneath all of these individual flaps is too extensive a series of procedures to undertake, when the end-results are so poor. The finger is pulled into extreme flexion, and often dislocation, when the extensor has been destroyed. This deformity can only be corrected by fusion of the affected joint, usually the proximal interphalangeal, in moderate flexion. The alternative is amputation of the terminal one or two phalanges when they interfere with gripping objects with the fingers. The working man usually prefers the latter solution, especially when the involved digit is the little finger. In many cases, the tip of the finger is so covered with scar, and is so contracted, with useless joints, that it is painful and useless and is better amputated.

The circulation of the burned hand is often poor, and the relief afforded by skin-grafting, while very great, is often insufficient to restore normal circulatory balance, particularly when the hand has been atrophied from long disuse. Such hands remain blue and cold, and the return of function is extremely slow. Since sympathetic block will, at times, give temporary relief of this condition, it may be possible that sympathectomy should be performed in these intractable cases.

Pigmentation of the skin-grafts after application remains an unsolved problem, and all too often a good functional result is marred by the poor color match of the grafted skin (Fig. 5). Many of these will improve with time, but in certain individuals the pigmentation is permanent. Fortunately, such pigmentation occurs rather infrequently. It is much more common in brunettes than in blondes, but can occur in either.

SUMMARY

The chief characteristic of normal skin on the dorsum of the hand is elasticity. Burns destroy this function and it can be returned only after replacement with new, elastic skin-grafts which replace the inelastic scar. The object of the surgeon is to close the granulating wound as rapidly as possible. Poor marginal scars, contraction of the bed, and the need for frequent secondary revisions have led to the adoption of simple skin-graft technics for "temporary" epithelization of the wound. Late repair can then be performed on a healthy patient as an elective procedure when the wound is sterile, allowing extensive dissection and removal of all scar-tissue. Methods of repair are discussed and several unsolved problems in this field of surgery are enumerated.

REFERENCES

[1] Brown, J. B., and McDowell, F.: Skin-Grafting of Burns. Phila., J. B. Lippincott, 1943.

2 Blair, V. P., and Byars, L. T.: Treatment of Wounds Resulting from Deep Burns. J. A. M. A., **110,** 1802, May 28, 1938.

3 Bunnell, Sterling: Surgery of the Hand. Phila., J. B. Lippincott, 1944.

4 Converse, J. M.: Skin-Graft of Dorsum of Hand. ANNALS OF SURGERY, **121,** 172, February, 1945.

5 Davis, J. S.: The Use of Small Deep Grafts in the Repair of Surface Defects. Amer. J. Surg., **47,** 280, February, 1940.

6 Farmer, A. W., and Woolhouse, F. M.: Resurfacing of Dorsum of the Hand Following Burns. ANNALS OF SURGERY, **122,** 39, July, 1945.

7 Harkins, H.: The Fluid and Nutritional Therapy of Burns. J. A. M. A., **128,** 475, June 16, 1945.

8 Harkins, H.: The Present Status of the Problem of Thermal Burns. Physiol. Rev., **25,** 531, July, 1945.

9 Jayes, P. H.: Burns of the Hand. Brit. J. Indust. Med., **1,** 106, April, 1944.

10 Koch, S. L.: The Transplantation of Skin and Subcutaneous Tissue to the Hand. Surg., Gynec. and Obst., **72,** 1 and 157, January and February, 1941.

11 Koch, S. L.: Surgical Cleanliness, Compression and Rest as Primary Principles in the Treatment of Burns. J. A. M. A., **125,** 612, July 1, 1944.

THE THORACO-ABDOMINAL CASUALTY

ROBERT H. WYLIE,
NEW YORK, N. Y.

HENRY L. HOFFMAN,
CLEVELAND, OHIO

DONALD B. WILLIAMS,
LAFAYETTE, LA.

AND

WILLIAM F. ROSE,
ST. LOUIS, MO.

THE SCOPE OF THIS REPORT is a discussion of the thoraco-abdominal casualty in the Forward Hospital, with a presentation of the available data from 903 case records of the 2nd Auxiliary Surgical Group during 1943, 1944 and 1945.

The thoraco-abdominal wound is defined in this report as a wound produced by a missile perforating the diaphragm with entrance into the pleural and peritoneal cavities. Casualties, in which the pleural cavity and peritoneum have been entered by separate missiles without injury to the diaphragm, have been excluded. However, a wound of the so-called "bare area" of the liver, incurred by a fragment entering through the chest and diaphragm has been considered a true thoraco-abdominal wound.

A comparison of the incidence of the thoraco-abdominal wound with respect to all abdominal wounds is of interest. During the period covered by this report, 3,532 operations upon abdominal wounds of all types were performed. The thoraco-abdominal wound comprised 25.5% of this group of abdominal cases.

The great majority of casualties presented are Infantrymen of the U. S. Army and of the Wehrmacht, with a scattered number of Allied British and French soldiers, and a few civilians. The age factor, then, is of little significance, because, of necessity these men were in the young healthy adult male group.

Artillery and mortar fire was responsible for 590 of the thoraco-abdominal wounds, and rifle, machine gun and pistol fire accounted for 245. The few remaining wounds were caused by bomb, mine and grenade fragments.

The pattern of entry of the fragments or bullets in thoraco-abdominal wounds shows that 837 of the missiles entered the abdomen through the thorax, against 66 which penetrated the chest through the abdomen. The entrance wound in the chest was equally distributed on the right and the left sides. Four hundred and eighteen (418) missiles entered through the right, and 419 through the left chest.

For the sake of maintaining continuity in presentation of data, and in discussion of points of practice, not covered by records, the report is divided into the preoperative, the operative and the postoperative phases.

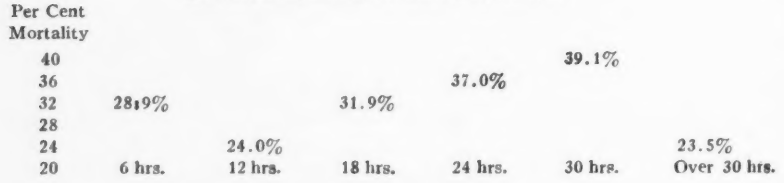
THE PREOPERATIVE PERIOD

The preoperative phase of the course and treatment of the casualty with a thoraco-abdominal wound embraces the time period from wounding to operation. It is the period of so-called "time-lag." This interval is concerned with the evacuation of the casualty from the battlefield to the hospital, the treatment of shock, the examination and diagnosis.

Time-lag for all patients, and for patients who died, is presented as the number of cases in each six-hour interval up to 30 hours, and for those that came to operation at any time after 30 hours. The percentage mortality shows a progressive increase after the first 12 hours, and drops again for those operated upon after 30 hours. The greater mortality in the period up to six hours is a reflection of the fact that the nearer to the front the Field Hospital is set-up, the higher the expected mortality, because with a short evacuation distance from the line, more of the desperately wounded patients will arrive in the hospital before dying. For example, all the patients in this series with wounds of the vena cava and portal vein are found in this period. The eight casualties that came to operation after 30 hours sustained wounds involving the liver in two cases, the spleen in three instances, the kidney once, and two cases had penetration of the peritoneal cavity without damage to a viscus.

TABLE I

THORACO-ABDOMINAL: 903 CASES—247 DEATHS



When these casualties were received in the first priority surgical hospital from the division clearing station, measures to combat shock and maintain respiratory equilibrium had already been instituted in the form of occlusive dressings to sucking wounds of the chest, injection of morphine, and infusion of plasma. On arrival at the hospital, 455 casualties with thoraco-abdominal wounds had received an average of 525 cc. of plasma each. One hundred and forty-four (144) patients had not received plasma before admission, and the records were missing on this point in 324 instances.

When first seen at the hospital on admission, the degree of clinical shock was recorded by the surgeon as "none," "mild," "moderate" or "severe," or its equivalent. With an increase in the severity of clinical shock on admission, there was a corresponding rise in the percentage of fatalities. There was

a 5.5% mortality in those casualties reaching the hospital without clinical evidence of shock, whereas 59.6% of all cases that arrived in severe clinical shock, died subsequently.

In the shock tent of the hospital, replacement therapy was continued as indicated by the degree of shock and estimated blood loss. The usual practice in those cases requiring replacement treatment was to start an infusion of plasma immediately while waiting for blood to be cross-matched. Thereafter, therapy was continued with blood transfusion. Four hundred and eight (408) patients received an average of 500 cc. of plasma. Two hundred and fifty-two (252) casualties did not receive plasma, and in 353 instances there were no records of it. Similarly, 619 patients received an average of 1100 cc. of blood in the shock tent, while 60 casualties did not get any. Records were lacking on transfusion in 224 instances.

The intelligent regimen of resuscitation and treatment depends on the early recognition of the wound as thoraco-abdominal in extent. Hence, one prompt and thorough examination to discover the site of all wounds, and their position relative to the diaphragm, is paramount. For practical purposes, any perforating fragment which crosses the horizontal zone bounded by the plane of the costal margin and 12th rib below, and the line between the nipple and the angle of the scapula above, may perforate the diaphragm. Where a penetrating wound was present, roentgenologic examination was a necessity. Anteroposterior and lateral positions, preferable in the sitting position for the chest, and with an overexposure of the film for both abdomen and chest, was important to check the position of the retained fragment or bullet, with the site of entry. By this means an effort was made to determine whether or not the zone of the diaphragm had been perforated. Elsewhere roentgenograms were of practical use only in confirming the presence of mediastinal shift associated with an hemothorax or a pneumothorax, and of fractured ribs.

Further clinical examination of the casualty was directed at an evaluation of the cardiorespiratory status—the presence of cyanosis, respiratory restriction due to pain, embarrassing hemothorax or pneumothorax, and excessive tracheobronchial accumulation of blood and mucus. When present, these were treated in the preoperative period by oxygen through a nasal catheter or mask, by intercostal nerve block with procaine, by aspiration of blood and air from the pleural cavity, and by tracheal aspirations with a catheter. The effect of these measures upon cardiorespiratory imbalance and upon the shock state itself was gratifying in a high proportion of cases.

However, in thoraco-abdominal wounds less time could be devoted to stabilization of the cardiorespiratory physiology than in the purely thoracic cases. Of prime importance in combating shock, and saving life in thoraco-abdominal wounds was early operative treatment. There is always the probability that contamination of peritoneum and pleura is present, and this, with continued hemorrhage, constitutes the main causes of continued shock and threat to life. Temporizing and delay in bringing these patients to early operation, as soon as replacement therapy had been started, diagnosis estab-

lished, and measures to combat serious cardiorespiratory imbalance performed, should not be permitted. Even in those patients whose response is poor to adequate treatment, delay in the preoperative tent should, ideally, never exceed two or a maximum of three hours. The operative procedure itself, with control of respiration under endotracheal anesthesia and tracheal aspiration, closure of the chest and diaphragmatic wounds, and, finally, control of hemorrhage and contamination, is the ultimate treatment of shock in these patients. It should not be postponed.

Further clinical examination of the abdomen is relatively unimportant, and often hard to evaluate, because of referred tenderness and pain with the accompanying chest wound, and rigidity associated with respiratory difficulty. Of importance, however, in the preoperative treatment is the introduction of a nasal stomach tube for aspiration of gastric contents. By this means not only is the stomach drained to minimize vomiting during operation, but also the presence of large amounts of blood in the aspirations was of diagnostic significance. Dilation of the stomach with air, to such a degree as to be a factor in the embarrassment of respiration, was not an uncommon finding in these patients, and relief, on occasion, was striking, following aspiration. The stomach tube was fixed to remain in place and drain during operation. In addition, an examination of the voided or catheterized urine for the presence of blood was made in the preoperative period. This gave valuable information as to the course of the missile in relation to the kidney. Before finishing a discussion of the preoperative period it must be emphasized that in some chest wounds, it was impossible to decide whether or not the diaphragm had been perforated. These cases were treated as any suspected wound of the abdomen, and a thoracotomy performed to explore the diaphragm for perforation.

OPERATIVE PERIOD

With the movement of the casualty from the "shock" tent to the operating tent by stretcher the operative phase of this report is entered. In the majority of instances the patient was operated upon on the stretcher, thus, eliminating the awkward, and not harmless procedure of moving a desperately wounded patient at the outset, and conclusion of the operation. This phase in the care of the thoraco-abdominal casualty deals with the anesthesia, pathology, operative approach, and procedure.

The average length of time under anesthesia for patients with thoraco-abdominal wounds was slightly over 2.5 hours. The majority of inductions were performed with nitrous oxide and oxygen. Ethyl chloride, ether alone, or sodium pentothal were employed to induce the patient in a few instances each. In nearly all cases, maintenance anesthesia was achieved by endotracheal ether and oxygen in a closed circuit. This is the anesthesia of choice. It is impossible to overestimate the value of endotracheal anesthesia in operations upon thoraco-abdominal wounds. The anesthetist, who is an expert in the technic of endotracheal anesthesia, must also appreciate the importance of frequent and thorough catheter aspiration of the tracheobronchial tree. This

was performed before, often during, and always at the termination of the operative procedure. In addition, the value of positive pressure anesthesia, during the period of operation when the thoracic cavity is open, and during closure of the chest when reëxpansion of the lung was required, must be stressed.

There should be no hesitation in the use of bronchoscopy where the above technics have failed in effecting reëxpansion of the lung and reduction of blood and mucus in the tracheobronchial tree. One hundred and ten bronchoscopies are recorded as having been performed at the end of operation in this series of thoraco-abdominal wounds.

Replacement therapy, continued during operation, consisted of blood transfusions, and infusions of plasma and 5% glucose in saline. Six hundred and thirty-nine (639) patients received an average of 1000 cc. of blood during operation, and, in addition, 166 of these were given an average of 575 cc. of plasma each. Seventy-eight (78) patients were each given 1000 cc. of 5% glucose in saline during the course of the operative procedure as a supplement to plasma and blood. During 116 operations, no replacement was deemed necessary. One hundred and thirty (130) records do not treat with this point.

Before dealing with the operative approach and procedure in these thoraco-abdominal wounds, a discussion of the pathology encountered will be presented.

As stated above, the wound of entrance in the thoraco-abdominal casualty was in the thoracic cage 837 times, as against 66 instances in which the abdomen was the site of entry. In most instances, the injury to the chest wall was associated with fractured ribs. The fractured ribs roughly corresponded, to the zone of the diaphragm. In only three instances, of the ribs reported as fractured, was the site above the 6th rib posteriorly or the 4th rib anteriorly. The small size of the target, and the lethal effect of a missile entering the chest from a cephalad direction probably contributed to the paucity of cases with entry wounds in the upper chest.

Likewise, in most instances the described wound of the lung was in either lower lobe, with some cases of injury to the middle lobe on the right, and the lingula of the upper lobe on the left. The pathology in the lung at these sites was described as "contused" "containing hematoma" or as "perforated" or "lacerated." Because of the path of the missile through the lower part of the chest in the diaphragmatic zone, the peripheral portions of the lower lobes, and less frequently of the middle lobe and lingula of the left upper lobe, were injured.

The injury to the diaphragm falls roughly into three categories: the single or double small perforating wounds, the large lacerated wounds, and the avulsion of the diaphragm from its chest wall attachment. Similar to the chest wall, the right and left diaphragms were wounded quite equally. The right diaphragm was perforated in 435 cases and there were 448 wounds of the left. Both diaphragms were wounded in 20 instances. At the time of operation, evisceration of abdominal contents through the diaphragm was recorded to

have occurred in 57 cases. In 17 instances omentum alone protruded into the pleural cavity, but in 40 cases abdominal viscera were found in the chest.

The mediastinum was injured in 30 instances. The heart itself was wounded 14 times and the pericardium alone in 13 cases. The esophagus was injured once, and the posterior mediastinum twice.

In regard to the pathology in the peritoneal cavity, a consideration of the right and left diaphragm with their different underlying anatomic relationship, bears discussion. Wounds of the right diaphragm were associated in 407

TABLE II

FREQUENCY OF WOUNDING AND MORTALITY OF VISCERA AND COMBINATION OF VISCERA IN 903 THORACO-ABDOMINAL WOUNDS

	Total Cases	Fatal Cases	Per Cent Mortality
Liver	297	35	11.7%
Spleen	95	10	10.5%
Liver and kidney	59	14	23.7%
Spleen and stomach	43	18	41.8%
Liver and stomach	30	11	36.6%
Peritoneal cavity only	26	3	11.5%
Spleen, kidney	27	4	14.8%
Spleen and left colon	19	4	21.0%
Left colon	18	6	33.3%
Spleen, kidney and left colon	12	6	50.0%
Liver, spleen and stomach	11	3	27.2%
Spleen, stomach and left colon	8	4	50.0%
Spleen, kidney and stomach	9	3	33.3%
Liver and small intestines	9	1	11.1%
Liver, stomach and colon	8	5	62.5%
Liver, kidney and right colon	5	4	80.0%
Liver, small intestine and left colon	6	5	83.3%
Liver, stomach and biliary tract	6	4	66.6%
Kidney	11	4	36.6%
Stomach and left colon	8	2	25.0%
Spleen and small intestine	9	0	00.0%
Liver and spleen	7	3	42.8%
Stomach, small intestine and colon	8	2	25.0%
Small intestine and left colon	6	3	50.0%
Liver and right colon	7	4	57.1%
Kidney and stomach	4	1	25.0%
Liver and left colon	3	1	33.3%
Spleen, stomach and pancreas	3	2	66.6%
All other combinations	115	73	63.4%
(62 in all—mortality of 5 organs or more—100%)			

out of 435 times with a wound of the liver. The liver, then, was the organ which took the impact of the missiles entering through the right diaphragm. After the liver, the following organs in order of frequency, were wounded; the right kidney, the colon, the stomach, the small bowel, the duodenum, and the gallbladder. On the left side, the spleen, stomach, and colon were wounded most frequently, and received the impact of most missiles coming through the left diaphragm. In 448 wounds of the left diaphragm, the spleen was injured 272 times, the stomach 167, and the colon in 145 instances. The liver and

left kidney were wounded an equal number of times, followed by the small intestine and pancreas, in order of frequency. A comprehensive list of the frequency of organs and combinations or organs wounded is presented from the records (Table II).

TABLE III

31 TRANSDIAPHRAGMATIC PROCEDURES IN WHICH THORACOTOMY ALONE WAS EMPLOYED

Procedure	Total Cases	Fatal Cases	Per Cent Mortality
Liver drainage	148	17	11.4%
Splenectomy	87	9	10.3%
Splenectomy and stomach suture	27	12	44.4%
Stomach suture	23	5	21.7%
Colostomy (left colon flank colostomy)	12	3	25.0%
Splenectomy and colostomy	10	3	30.0%
Stomach suture and liver drainage	7	5	
Splenectomy—colostomy and jejunal repair	6	3	
Right nephrectomy and liver drainage	6	2	
Left nephrectomy and splenectomy	5	0	
Splenectomy, stomach suture and liver drainage	4	1	
Splenectomy, stomach suture and colostomy	3	1	
Stomach suture and colostomy	3	3	
Splenectomy and jejunal anastomosis	2	1	
Splenectomy, stomach and pancreas sutures	2	1	
Splenectomy and liver drainage	2	0	
Jejunal repair	1	0	
Left nephrectomy, stomach and jejunal repair	1	0	
Stomach suture, colostomy and liver drainage	1	0	
Left nephrectomy, splenectomy and colostomy	1	0	
Left nephrectomy and stomach suture	1	1	
Stomach suture, colostomy and liver drainage	1	0	
Left nephrectomy, splenectomy and stomach suture	1	1	
Stomach, small intestine suture and colostomy	1	1	
Jejunal suture, colostomy and liver drainage	1	1	
Stomach and jejunal suture	1	1	
Splenectomy, stomach suture, colostomy and liver drainage	1	0	
Left nephrectomy	1	0	
Left nephrectomy and stomach suture and colostomy	1	1	
Colostomy and liver drainage	1	0	
Left nephrectomy, jejunal suture and colostomy	1	0	
	369	0.72	19.9%

TABLE IV

METHOD OF OPERATIVE APPROACH AND MORTALITY IN 903 THORACO-ABDOMINAL WOUNDS

	Total	Deaths	Per Cent Mortality
Thoracotomy, with transdiaphragmatic celiotomy	448	91	20.3%
Celiotomy only	202	77	38.1%
Thoracotomy, then celiotomy	144	36	26.0%
Celiotomy, then thoracotomy	74	26	35.1%
Thoracotomy first, with transdiaphragmatic procedure followed by celiotomy	20	7	35.0%
Thoracoceliotomy traversing chondral arch	6	3	50.0%
Nonoperated	3	1	33.3%
Died before end of operation	6	6	100.0%

The anatomic relationships below the diaphragm have a direct bearing upon the operative approach and procedure on the right and left side. A tabulation of the types of approaches, that were used in 903 cases is presented from the records.

Any discussion of methods of approach must be qualified at the onset by saying that no one approach is ideal for all patients, but the judgment of the surgeon, knowing the individual patient, and his own capabilities, will decide the approach to be used by him. In general, where a thoracotomy and celiotomy were both contemplated, the chest procedure was performed first, because the patient stood a celiotomy better after the chest wall and diaphragm had been closed and the lung reëxpanded.

In other words, a more balanced cardiorespiratory system is an important measure in combating shock, and thoracotomy should be performed before, rather than after, a long abdominal procedure.

The practice of stabilizing the chest operatively, by closure of the chest wall and diaphragm, and removal of blood with reëxpansion of the lung, before attempting other procedures is a principle of attack about which there can be little disagreement. The question of how much surgery should, or can be done through the chest and diaphragm, and how much through the abdomen, is open to discussion. In this series, 362 cases with thoraco-abdominal wounds had the entire abdominal procedures performed through the diaphragm. In this group, 31 different combinations of organs were operated upon (Table III).

In further discussion of this topic a consideration of the possibilities of approach when the wound is on the right or on the left side will be debated. Perforating wounds of the chest on the right side, in the upper zone of the diaphragm, are more satisfactorily attacked through a thoracotomy incision, because the diaphragm is much more readily sutured from above, than from below. The presence of the liver makes adequate exploration and suture difficult, and often impossible from below the diaphragm. Similarly, penetrating wounds of the upper zone of the diaphragm, in which the foreign body lies beneath the dome of the diaphragm well within the liver, are more easily handled by the thoracotomy-diaphragmatic route. However, on the right side, perforating or penetrating wounds of the lower zone of the diaphragm in the region of the costophrenic sinus, in which the tract of the missile may well have passed below the liver, should be attacked primarily by a celiotomy approach. Débridement and closure of the chest wall may be done first, or second, depending upon the urgency of the suspected abdominal pathology, and the amount of respiratory embarrassment present. The diaphragm may be closed by either route in the region of the costophrenic sinus, except posteriorly, where closure was difficult, and sometimes impossible from the abdominal cavity. Through the transdiaphragmatic approach on the right side, the field of exploration of the abdomen was limited to the superior surface of the liver, the right kidney, and the hepatic flexure of the colon.

On the left side, the problem is somewhat different, the absence of the liver mass, and the relationship of the fundus and body of the stomach, spleen,

splenic flexure of colon, body and tail of pancreas, and the left kidney to the inferior surface of the diaphragm, not only makes for easy accessibility to these organs through the diaphragm, but also permits greater facility of exploration and suture of the diaphragm from below. Wounds of the left diaphragm carry with them the threat of contamination of the pleural cavity through the diaphragmatic wound by stomach, colon, and small bowel contents.

The data collected from the records cannot be used to show the superiority of either the celiotomy, or the thoracotomy approach, separately in these cases. Depending upon the individual case the magnitude of the abdominal and the thoracic problem, the approach may be best by thoracotomy or by celiotomy, or by both. It may be said, however, in perforating wounds in the upper zone of the left diaphragm, or in penetrating wounds in which the fragment on roentgenologic examination can be demonstrated to lie within the area of the dome of the diaphragm, that these patients may be treated with facility through the thoracotomy-diaphragmatic approach. In these cases the expected injury was a perforation of the spleen, stomach, or kidney, all of which organs are accessible to surgery through the diaphragm. Likewise, wounds of the splenic flexure of the colon may be exteriorized in the flank through this exposure. In addition to these organs it must be stated, that exposure of, and operation upon, most of the transverse colon, the upper part of the descending colon, and the small intestine from the ligament of Treitz to within 18 inches of the ileocecal junction, can be performed through the left diaphragm, depending somewhat upon the habitus of the patient, and the length of the mesenteries.

In those instances of perforation of a hollow abdominal viscus, particularly where there is a diaphragmatic wound of any size, a thoracotomy is distinctly of advantage before a celiotomy, in order to cleanse the pleural cavity of gross contamination. In fact an important part of any thoracotomy entails removal of all foreign material and clot, with a thorough irrigation of the pleural cavity with saline solution. However, in those cases in which a small perforation in the diaphragm is present, and in which contamination is minimal, it must be considered whether it is wise to widely open the diaphragm to attack perforations of hollow organs, thus exposing the pleura and chest wall to wider contamination. These are some of the problems that are met, and which must color the judgment of any surgeon required to meet them.

Further discussion of operative procedure will be limited to the problems peculiar to the thoraco-abdominal wound. Thoracotomies, as performed on these cases, were of four types: (1) A limited thoracotomy achieved by extending the missile wound; (2) a thoracotomy through the area of the wound; (3) a thoracotomy outside the area of the wound; and (4) a so-called combined thoraco-abdominal incision, in which the thoracotomy was extended through the costal arch and down through the abdominal musculature. In the first category are found those in which the chest wound to be débrided was large, and by simple extension of this wound adequate exposure and suture of the diaphragm could be carried out. In Groups 2 and 3, are the majority of cases. They comprised those in which a formal approach was performed, usually

posterolaterally, and either through the rib bed of the 9th rib or the 9th intercostal space. A small proportion of these thoracotomies were performed laterally in the region of the 6th and 7th spaces. Approximately, twice as many of these thoracotomies were performed through the intercostal space as through the bed of a rib. The exposure which gave the best approach to transdiaphragmatic work was the posterolateral one, in the region of the 9th or 10th ribs. The combined approach, of which there were six recorded, was used in two cases in which the costal margin had already been destroyed by the missile. In the four cases in which it was employed as an elective approach one case resulted in a fatal infection, breakdown, and disruption of the wound. Nothing can be said in favor of this type of approach, as an elective procedure.

In this series of cases, records of procedures performed upon the lung included 80 instances in which lung suture was done, and two instances where a segment of the right lower lobe was excised. Records of removal of foreign bodies from the lung were found in nine cases.

The method of opening the diaphragm for exposure of abdominal viscera was not specifically stated in the records, more than that the "wound was extended" or, in case of two wounds, that they "were connected by incision." As stated above, the missile wound or wounds in the diaphragm were utilized in the performance of a more extended opening in the diaphragm. The direction and extent of incision will depend upon the site of the suspected or known viscera wounded, and the amount of exposure necessary.

The closure of the diaphragm is of utmost importance in these cases, both on the right, and on the left. Suture of the left diaphragm is imperative to cut-off the path of contamination and infection from the peritoneal cavity, and to prevent herniation of abdominal viscera into the pleural cavity. It is, likewise, mandatory to close the right diaphragm to prevent the occurrence of bile pleuritis and empyema, and also to keep contamination and infection from invading the pleural cavity. Even in those instances in which a small fragment has penetrated the liver through the diaphragm, it is conservative to explore, suture the diaphragm, and drain the liver, because it is impossible to estimate in every case the size of the diaphragmatic laceration or liver injury from the size of the missile. In some instances, particularly where a rib has been fragmented in passage of a small missile, it is surprising to find the extent of diaphragmatic and liver laceration.

A firm closure in the greatest proportion of these cases was insured by interrupted silk sutures. In those cases in which the diaphragm was avulsed from the chest wall, it was secured by transplantation and suture at a higher level on the chest wall. The phrenic nerve is recorded as having been crushed in 11 instances.

Discussion of the specific treatment of individual organs of the abdominal cavity is not the province of this report. Suffice it to say that wounds of the stomach and duodenum were sutured, wounds of the colon were exteriorized, wounds of the small bowel treated by suture or by resection and an anastomosis, of the spleen by splenectomy, and of the liver by subcostal drainage. Wounds

of the kidney were treated by nephrectomy, only when hemorrhage was persistent, or the pelvis involved, otherwise drainage sufficed. Treatment of the pancreas was by suture and drainage, or by drainage alone. The celiotomy incision was either a right or left rectus, and closure invariably entailed some type of retention suture.

Detailed complete information in respect to closure of the thoracic wound was not present in the records. In general, closure of the thoracic cage was accomplished by approximation of adjacent ribs or intercostal musculature, depending on whether the thoracotomy was performed through the intercostal space or the bed of a rib. In the case of thoracic wall defects, utilization of contiguous musculature in layers was the usual method employed. Closure of the muscle layers of the chest wall was performed with, or sometimes without, closure of subcutaneous tissue and skin. As already emphasized under anesthesia, one of the most important parts of closure is the reëxpansion of the lung by the anesthetist utilizing positive pressure. In order to achieve complete exhaustion of air and fluid in the pleural space, either catheter suction just prior to closing the chest, or needle aspiration after closure were useful.

Three hundred and twenty-six (326) cases were recorded as having been drained by a closed water-trap intercostal catheter or tube. Either a large-sized fenestrated catheter, or tube of equal caliber, with enough rigidity to prevent it from collapsing, was the available material most commonly used for drainage. The site of drainage was usually the posterolateral or lateral aspect of the lower chest through a separate intercostal stab wound. In a few instances a small catheter, in addition was placed in the 2nd interspace anteriorly.

A discussion of the question of whether drainage should be required in these thoraco-abdominal wounds, leads to a consideration of the extent of the lung damage, the defect of the chest wall, the magnitude of the diaphragmatic perforation, and the presence of gross contamination from the wound, or particularly, through the diaphragm from a perforated abdominal viscus. Only in those cases in which the thoracic wall defect is small, and in which lung and diaphragmatic injuries are minimal, without gross contamination, may water-seal intercostal drainage be disregarded as a factor in postoperative expansion of the lung by elimination of pleural blood and air, and control of transient bronchopleural fistulae. The rôle of the intercostal catheter drainage in control of pleural infection is that by elimination of the pleural dead space, the process is limited and localized. It is pertinent to stress that the care of the water-trap drainage in the postoperative period requires constant vigilance on the part of the surgeon, and a thorough knowledge and conscientious attention on the part of the nursing and corpsman staff of a first priority surgical hospital.

THE POSTOPERATIVE PERIOD

The records of the various phases of postoperative care are incomplete in respect to the various details, so that a discussion must be given of the problems encountered. In general, the care of the patient with a thoraco-abdominal wound entails attention to details of care common to both the chest and the abdominal patient.

Complications recorded in order of frequency were atalectasis, empyema, subphrenic abscess and pneumonia. Bronchopleura fistula was reported four times—twice with empyema, and twice with a bile empyema. Pressure pneumothorax occurred in three instances as a postoperative complication.

The postoperative care of the chest is directed towards maintaining cardiorespiratory balancé, promoting expansion of the lung, and removal of blood and air from the pleural cavity to allow full expansion and minimize the chances of pleural thrombus formation. When these patients are brought into the postoperative tent, some will need oxygen and additional blood, as indicated by cyanosis and signs of peripheral circulatory failure. As soon as the patient is conscious, he should be started on a regimen of frequent turning from side to side, with insistence upon deep breathing and coughing. If the patient cannot, or will not cough, and raise the blood and mucus, intercostal block and tracheal aspirations by catheter should be instituted early and repeated as frequently as is necessary in the presence of atelectatic areas in the lungs, or detectable amounts of blood or mucus in the tracheobronchial tree. Often after the first tracheal aspiration the patient will cough and raise without protest. In the event that these methods do not avail in the presence of a pulmonary collapse, bronchoscopy should be employed. There are records of the use of bronchoscopy in 12 instances in the postoperative period. The advantage of the thoracotomy wound alone, without celiotomy, was distinctly appreciated in the postoperative period. The absence of an abdominal incision made for more comfort and for better coöperation from the patient in his important part in lung expansion.

It was the general practice to continue water-trap intercostal tube drainage of the chest for two to three days. Often these tubes did not function efficiently for this period, but became sealed-off after 24 hours. After removal of the tube on the 2nd or 3rd day, and before, in cases without drainage, aspiration of blood and air was done as indicated, daily if necessary. Often a pocket of air was encountered anteriorly, even in those patients who had a lateral or posterolateral intercostal tube. This was evacuated by aspiration with a needle as soon as detected. Morphine in doses larger than 0.25 grain should not be given to these patients, and its use should not be on a routine basis. One-sixth of a grain in many instances sufficed to control the pain in these patients.

A detailed discussion of the postoperative care directed at the abdominal part of the wound will not be entered into in this report, except to emphasize the importance of nasal tube stomach siphonage. All these cases particularly with hollow viscus injury should have a nasal tube stomach drainage for varying periods up to four days, depending upon the reëstablishment of peristalsis to the surgeon's satisfaction. Use of stomach siphonage indiscriminately beyond the period of four days may veil a bowel obstruction, and delay recognition and correction of it.

An accurate knowledge of the daily intake and output of the patients is imperative. During the period in which nasogastric siphonage was in use between 2,000 and 3,000 cc. of 5 per cent glucose in saline was given to these

patients daily. Caution should be exercised in giving a total amount of parenteral fluids in excess of 3,000 cc. daily because of the impaired cardiorespiratory reserve which may exist, and the possibility of producing pulmonary edema. The amount of replacement in blood and plasma given in the postoperative period should be guided by hemoglobin hematocrit and serum protein determinations. A normal level should be reached as soon as possible. The routine employment of vitamins B and C in the postoperative period was considered advantageous.

The use of sulphonamide and penicillin therapy as employed in these cases from the time of wounding through the postoperative period was as follows. Sulphanilamide crystals were placed in the fresh wound in the battalion aid station throughout the entire period. During 1943 and up to May of 1944 sodium sulphadiazine was given parenterally in the postoperative period. After May, 1944, penicillin was instituted and was given intramuscularly in doses which varied between 20,000 and 25,000 units at a three-hour interval, starting in the shock tent and extending through the postoperative period. Before May, 1944, five or ten grams of sulfanilamide crystals were placed in the pleural cavity before closure of the chest in most cases and, after May, 1944, penicillin in amounts ranging from 30,000 to 50,000 units were used similarly in the majority of instances. The use of sulphonamide and penicillin in the abdominal cavity was not as uniform. In most instances their use depended upon the perforation of a hollow viscus. Before May, 1944, five or ten grams of sulphanilimide crystals were left in the peritoneal cavity and, after May, 1944, about one-half of the cases still received sulphanilamide crystals, and one half 50,000 units of penicillin intraperitoneally. Due to the lack of follow-up in the survival patient, it is impossible in this report to give any definite data referable to the relative rôle these drugs played in prevention and control of infection.

TABLE V

MORTALITY RATE—903 THORACO-ABDOMINAL WOUNDS

(*First-Priority Surgical Hospital only*)

	Total	1943	Jan.-Jun. 1944	Jul.-Dec. 1944	1945
Number of cases	903	68	243	392	200
Number of deaths	247	25	84	98	40
Per cent mortality	27.3%	36.7%	34.9%	25.0%	20.0%

Before dealing more fully with mortality, it is pertinent to recognize that the lower mortality rate for these patients in the latter half of 1944, and the year 1945, coincides with the era of penicillin. Without proof, nevertheless, it is considered that this reduction in mortality is a reflexion, more likely, of a greater knowledge and experience in dealing with the problem of the thoraco-abdominal wound as a whole, a greater appreciation of the thoracic implications and complications, a greater experience and facility of the individual surgeon and anesthetist in the operative treatment, and, lastly, a keener appreciation and attention to details of preoperative and postoperative care.

The gross mortality for the 903 cases with thoraco-abdominal wounds was

246, or 27.3 per cent. For 1943, the fatalities were 36.7 per cent for the first six months of 1944, 34.9 per cent, for the last half of that year, 25 per cent, and for 1945, 20 per cent. These mortality figures are for deaths in the first priority surgical hospitals, where the usual postoperative residence was from seven to ten days. Some cases remained in this hospital only a few days, while some stayed as long as 18 days.

It is impossible in the analysis of the mortality data to discover what effect the chest component of the wound had upon mortality except in the case of the wounds injuring the mediastinum. The mortality when this part of the chest was wounded was 50 per cent.

TABLE VI

RECORDED COMPLICATIONS IN 656 THORACO-ABDOMINAL WOUNDS—SURVIVAL CASES

	No. of Cases
Atelectasis	21
Empyema	17
Empyema with bronchopleural fistula	2
Subphrenic abscess	15
Pneumonia	12
Abdominal wound disruption	7
Abdominal wound disruption, with evisceration	3
Bile empyema	5
Bile empyema, with bronchopleural fistula	2
Chest wound infection and breakdown	8
Intestinal obstruction	5
Persistent pleural effusion	5
Tension pneumothorax	3
Jaundice	3
Incomplete expansion of lung	2
Oliguria	2
Gastric hemorrhage	2
Chest wall and diaphragm breakdown	1
Psychotic state	5
Leg vein thrombosis	2
Hepatic abscess	1
Pelvic abscess	1
Pulmonary edema	1
Hemorrhage from thoracotomy wound	1
Pulmonary embolism	1
No complications recorded	364
No records	165
	656

However, the most lethal part of the thoraco-abdominal wound was the abdominal portion. Roughly, the type of organ and number of organs wounded below the diaphragm was reflected in the mortality rate. Wounds involving five or more different organs were universally fatal.

The mortality rate of all abdominal wounds in the first-priority surgical hospitals as compared to the thoraco-abdominal wound is of interest. In abdominal wounds of all types there was a mortality rate of 24.1 per cent, in the thoraco-abdominal wound the rate was 27.3 per cent. This covers the entire period of 1943, 1944, and 1945 in the case records of the 2nd Auxiliary Surgical Group.

The cause of death and postoperative day on which death occurred were recorded in 234 out of 247 fatalities. Shock was given as the most frequent cause of death on the operating table, the day of operation, and the first postoperative day. Four (4) cases were recorded as having died on the operating table of hemorrhage. However, in the so-called shock death, blood loss was a contributory factor, as were overwhelming contamination and infection of the peritoneal and pleural cavities and retroperitoneal space, disturbance of cardiorespiratory physiology, and massive tissue destruction. In 15 cases renal

TABLE VII

MORTALITY-TIME POSTOPERATIVELY AND PRIMARY CAUSE OF DEATH

(247 Deaths—13 Cases no Records)

Time and P.O. Day	Number of Deaths	Shock	Hemorrhage	"Renal Failure" Oliguria and Anuria	Atelectasis	Pneumonia	HT. Tamponade or Injury	Peritonitis	Missed Perforation	Peritonitis and Pleuritis	Pulmonary Emboli	Mismatched Blood	Blast	Mediastonitis	Fat Embolism	B-P Fistulae (Pressure pneumothorax)	Liver Deaths	Gas Infection	Disrupt. Diaphragm	Morphinism	Bronochoscopy	Meningitis	Liver abscess	Empyema
On operating table....	49	40	4		3		1														1			
Operative day.....	76	59					2	6	2	2	1	1	2							1				
1st P. O. day.....	29	18			1	2		2		2	2		1	1										
2nd P. O. day.....	28	12			1	7		4			2				1							1		
3rd P. O. day.....	12	1		5	2			1			1					2								
4th P. O. day.....	9			4		3											1	1						
5th P. O. day.....	7			4		1		2																
6th P. O. day.....	7					2		1			1							1	1					1
7th P. O. day.....	6			1		2		1			1													1
8th P. O. day.....	3							1																2
9th P. O. day.....	3			1							1												1	
10th P. O. day.....	2							1			1													
11th P. O. day.....	0																							
12th P. O. day.....	0																							
13th P. O. day.....	2							1																1
14th P. O. day.....	1																		1					
	234	130	4	15	7	17	3	20	2	4	10	1	3	1	1	2	1	2	2	1	1	1	1	5

failure, as expressed in oliguria and anuria, was the cause of death most commonly encountered from the 3rd to the 5th postoperative. Peritonitis and pneumonia were the next most frequent cause of fatalities, respectively.

In nine cases, death was considered to have been due to the effect of an associated injury rather than as a result of the thoraco-abdominal wound. The rôle of the associated wound in the morbidity of these patients is an important factor. Lesions of the spinal cord, produced by the missile of the thoraco-abdominal wounds, have been considered as associated wounds. There were 95 severe, 129 moderate, and 161 mild associated wounds. The severe wounds included brain, cord, other chest, abdominal, fractured femur and amputations. The moderate group included fractures of long bones other than the femur, and multiple wounds of less serious nature than those of the severe category.

Flesh wounds and those involving fractures of the hand and foot are listed under mild wounds.

CONCLUSIONS

1. Recognition of perforating wounds of the diaphragm in chest and abdominal casualties is of prime importance.

2. The value of correction of altered cardiorespiratory physiology in the preoperative period, of endotracheal anesthesia during the operation, and of reëxpansion of the lung at operation and postoperatively cannot be overestimated in the treatment of those patients.

3. The importance of early operation because of the abdominal wound, and of initial control of the thoracic pathology at operation upon the thoraco-abdominal wound is stressed.

4. The transdiaphragmatic procedure alone is a satisfactory method of approach in certain types of thoraco-abdominal wounds as demonstrated by the results of 362 procedures.

5. The reduction in the mortality of thoraco-abdominal wounds from 36.7 per cent, in 1943, to 20 per cent, in 1945, in the first-priority surgical hospital is the result of a fuller understanding of the problem of the thoraco-abdominal wound as a whole, of its thoracic implications in particular, of a wider experience of the individual surgeon and anesthetist, and of a keener appreciation of the essentials of preoperative and postoperative care. The rôle of penicillin cannot be estimated.